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Twenty-fourth Annual Convention
The Biltmore Hotel
Los Angeles, Calif., 20, 21, 22, 23 September 1959

Course in Postgraduate Gastroenterology
The Biltmore Hotel
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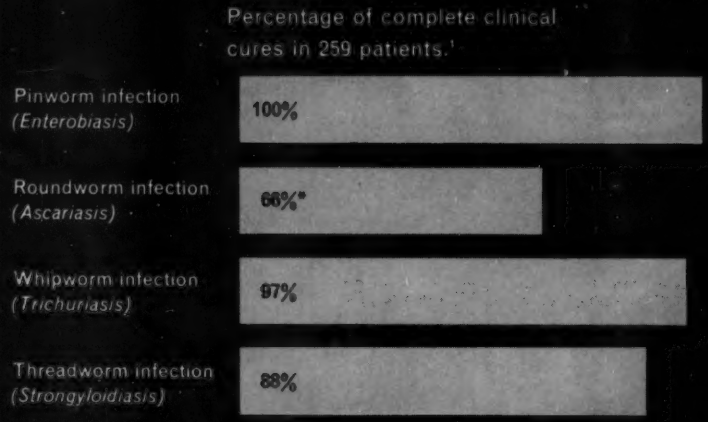

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1. Swartzwelder, J. C., et al.: J.A.M.A., 165:2063, 1957.

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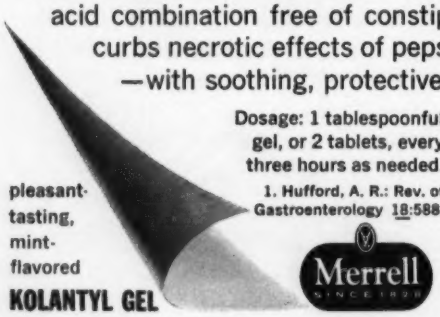

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1. Hufford, A. R.: Rev. of Gastroenterology 18:588.

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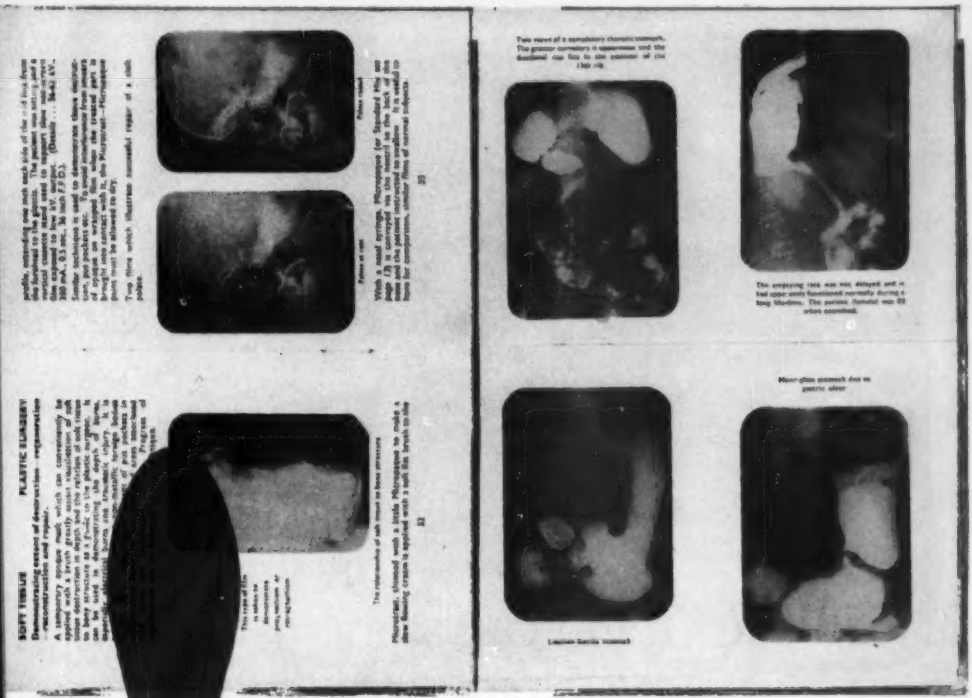

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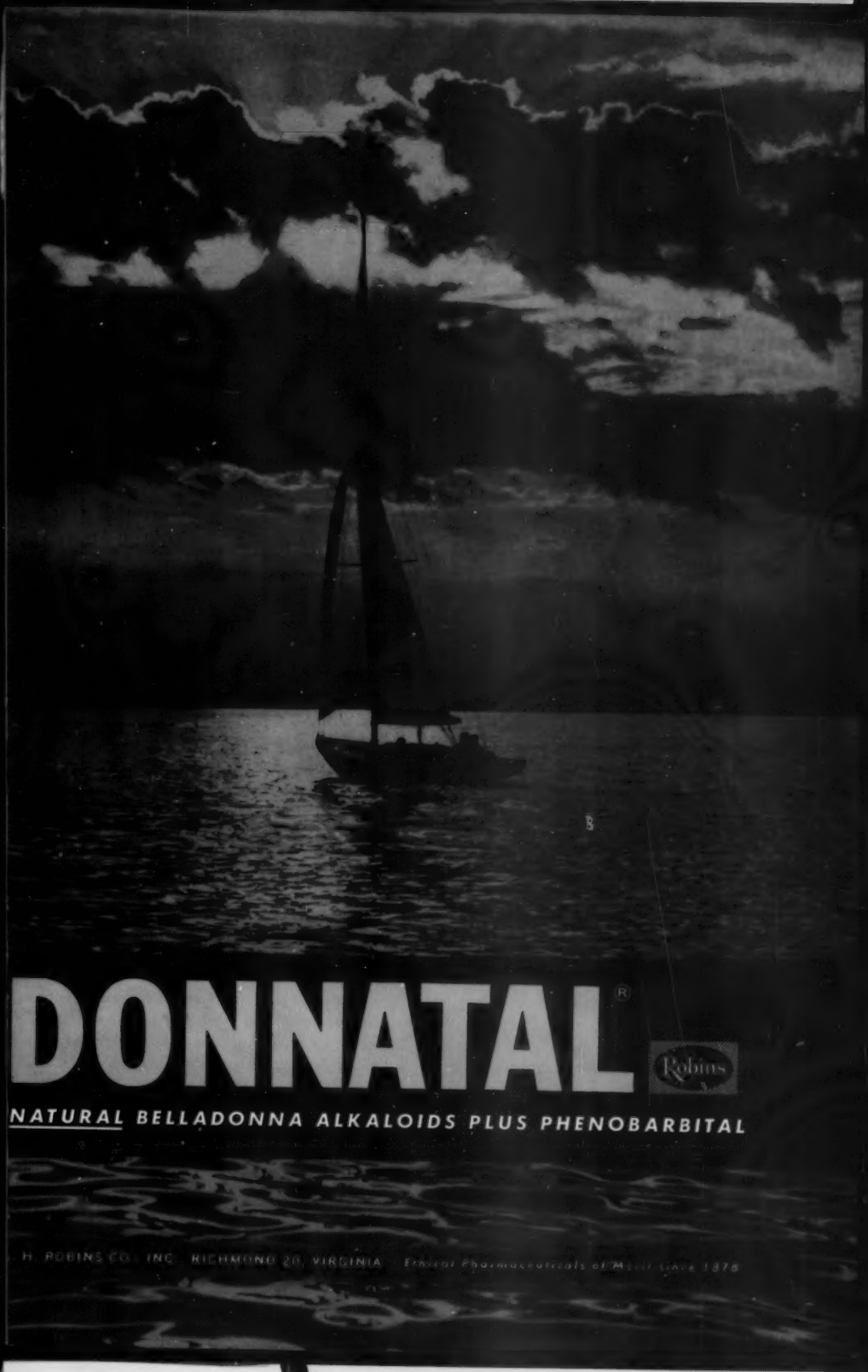
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VOLUME 32 SEPTEMBER, 1959 NUMBER 3

PANEL DISCUSSION ON FUNCTIONAL DISTURBANCES OF THE GASTROINTESTINAL TRACT*

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New Orleans, La.
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Rochester, Minn.
JOHN R. NEEFE, M.D., F.A.C.P.¶
St. Petersburg, Fla.
FRANK B. McGLONE, B.A., M.D., F.A.C.P.§
Denver, Colo.
and
HAROLD I. LIEF, A.B., M.D.‡
New Orleans, La.

Dr. Donovan C. Browne:—First, on behalf of the panel I wish to express our appreciation of the privilege of being here. It is indeed a privilege and I trust that our deliberations and discussions may add something to your knowledge. I am quite sure that it will add confusion, from what I have heard so far, but I think it will be worthwhile.

We are probably going to take a rather unorthodox course in conducting the panel and make it more or less informal.

At this point I wish to introduce to you the members of our panel.

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*Presented before the 23rd Annual Convention of the American College of Gastroenterology, New Orleans, La., 20, 21, 22 October 1958.

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¶Formerly Teaching Staff, Department of Medicine, Hospital of the University of Pennsylvania and University of Pennsylvania Medical School.
§Associate Professor of Medicine, University of Colorado.
‡Associate Professor of Psychiatry, Tulane University School of Medicine.

Dr. Frank B. McGlone, is from the city of Denver, Colo. He is Associate Professor of Medicine at the University of Colorado and Director of Medical Education at St. Joseph's Hospital.

To my immediate right, is Dr. J. Arnold Bargen. He needs no introduction to most of you. He is Professor of Medicine, Mayo Foundation, University of Minnesota, and Chairman of the Department of Gastroenterology, Mayo Clinic.

To my immediate left we have Dr. John R. Neefe of St. Petersburg, Fla., formerly of the teaching staff of the Department of Medicine, Hospital of the University of Pennsylvania and University of Pennsylvania Medical School; Staff Member, Mt. Park and St. Anthony's Hospital in St. Petersburg.

To my far left is Dr. Harold I. Lief of New Orleans, Associate Professor of Psychiatry, Tulane University School of Medicine. He has done extensive work among psychiatrists interested in certain somatic aspects and is known to most of you. He is visiting physician at Charity Hospital of Lousiana at New Orleans.

With this introduction of your panel, we will move on in our discussion of certain of the functional disturbances of the gastrointestinal tract. We are not quite so sure we agree on what is functional in contradistinction to simple psychosomatic disturbances. We have for decades had an increasing percentage of patients who present themselves with disturbances classified as functional, there being no demonstrable organic disease. This perhaps constitutes half or two-thirds of the patients seen in our practice.

Exactly why this has occurred? We hope we may find something of this today. It may be our industrialization, shifts in industrial areas and population with frustrations individuals experience playing a role, or we may have physicians who are better equipped, and our diagnostic armamentarium is improving. We will try to get some idea of the panel's thinking along this line, and see whether there is a plane of fundamental agreement or deep-seated differences of opinion. First, I wish to call on Dr. Bargen.

Dr. J. Arnold Bargen:—When one sums up the functional disturbances of the digestive tract, it becomes obvious that symptoms are most frequently referred to the intestinal tract. This would seem natural since the intestine occupies such a large portion of the digestive tract. Although these symptoms probably have no direct relation to the intestine itself, nevertheless, because of their location and the accompanying intestinal dysfunctions, they are given various names which indicate their relation to intestinal dysfunction. They are closely related to the anxiety problem.

I believe I am safe in saying that a measure of anxiety is probably present in all of us all of the time, or at least most of the time. As you sit here in this room, trying to listen to what is being said—and sometimes that is not too important—you are probably thinking about what is going on at the office, whether

your office girl is doing just what you told her, whether Mrs. Jones overcame her cholecystic attack that you left her with, and so on, and these are natural anxiety reactions.

The important question is, can anxiety become so severe that it can be transmuted into some pathologic process. It is known that intense emotional upsets involving marked anxiety are accompanied by physiologic changes. When the anxiety syndrome replaces mere anxiety, and the anxiety syndrome is persistent and elicited by inconsequential, inappropriate stimuli, it is indeed abnormal. Such an anxiety state may after a time arise subconsciously and be manifested by unusual functioning bodily states, resulting in vague, unrelated complaints in various organs and organ systems.

There is no part of the human anatomy in which these are more prevalent than in the region of the intestinal tract. Sometimes a single severe emotional impulse causes striking changes in the functions of an organ. I have seen an individual who was constipated all his life, develop diarrhea when the street opened in front of him during an earthquake in San Francisco. He had been to see me a month before, and I had outlined an anticonstipation program. He wrote me after the earthquake, saying: "Believe it or not, doctor, my constipation is cured." So, you see, an episode of fear, sudden and unwanted, can be an effective cure of a constipation.

The emotional effects of excitement and tension may be transient. When these distresses are frequently repeated, a tension state may develop resulting in marked change in intestinal function. Increased motility and decreased absorption of the *small* intestine are known to occur during an emotional state.

It is in the large intestine, however, where there has been much room for speculation about the effect of the psyche on intestinal function. Terms such as "unstable colon", "irritable colon", "spastic constipation", "atonic colon" are unsuitable to describe the actual state of affairs. They do express the general thought in regard to these intestinal disturbances. A condition is at hand in which emotional changes and a tension state have their profound effect. The condition which we usually describe as the "irritable colon" may not be particularly related to the colon. Sometimes there are symptoms, or manifestations, of overactivity or reduced activity of perhaps the entire digestive tract.

I daresay that most of the patients who walk into your office with disturbances of the digestive tract have symptoms commonly referred to as "the irritable colon". This may be the result of an emotional disturbance, a tension state, dietary indiscretions, or misuse of laxatives. I have no evidence, however, that it is ever followed by or related to actual intestinal disease.

Every gastroenterologist of some experience has seen the church leader, priest, or minister, the lawyer, the public speaker, who during or prior to his Sunday sermon or before delivering an important address, is afflicted with an

intense diarrhea. This condition largely subsides when the emotional strain is relieved. A mistaken diagnosis of colitis for these individuals is very unfortunate. There is no evidence, either clinical or experimental, to suggest that these disturbed emotional states ever produce an actual organic change in the intestine such as an inflammation, ulceration, or other irritation of the mucous membrane. It is well known that in some individuals, during unusual psychiatric stimulation, there has been produced hyperemia, or even edema and evidence of intestinal mucosal congestion. These promptly subside when the exciting stimulus is removed. They have never continued into the actual ulcerative intestinal state.

In recent years there has been an attempt to place conditions such as ulcerative colitis in the field of psychiatry. This is a very grave mistake. True enough, in some patients with ulcerative colitis, there is such a disturbed mental state that psychiatric help is needed. To approach the management of the disease itself, primarily on a psychiatric basis only, results in failure to help the patient and in misrepresentation of the facts by one physician to the other. It is important that each one of us maintains a sincere interest in the ability of the patient with ulcerative colitis to carry on. With patience, and sympathy, we must encourage him to sustain his affliction, not allowing him to become discouraged while active treatment of the condition is being carried on. In this, the psychiatrist can be of help. Outline of a positive program for the management of intestinal disorders, be they functional or organic, is of great importance and does much to alleviate the individual of his or her discomfort or suffering.

What I have said about ulcerative colitis applies to most of the functional disturbances of the digestive tract. A patient with these types of disturbances needs a very positive approach. The individual with digestive symptoms due to emotional aberrations is not well served when you say, "You might do this, or you might do that". Usually he has been plagued by uncertainty, and now he wants a positive program.

Now, some of the things I have said you naturally will ascribe to the fact that the old man has ideas which are unbendable, but I wanted to give you this. They come from a large experience with patients of all types of intestinal digestive disturbances in whom the largest portion of them has been of functional disorders, so when I speak of approaching these individuals in a positive way, I believe this is something that you should give some serious thought.

Dr. Browne:—Thank you, Dr. Bargen.

I think you gather from this statement that this is going to be a rather lively session. I wish you to note that on the tables before you are pads. We would be very pleased for you to write any pertinent questions and we will try to answer them in addition to those that we already have, as time will permit.

Now, with this statement, I think it is quite appropriate that we go to the far end of the panel, and ask Dr. Lief, our psychiatrist what he has to say.

Dr. Harold I. Lief:—To continue the discussion, I should like to present a point of view, a way of approaching these illnesses.

First, I should like to kick around one idea with you, and that is the idea of causality. Over and over again we hear physicians ask in regard to the patient who is ill, "What is *the* cause?"

I think we are approaching an era in science in which it is becoming more clear that there is no one single cause. As usual, the physical sciences lead the way in this approach. The physicists, for example, tell us that there are no causes for individual quantum transitions in the atom.

J. B. S. Haldane, the biologist, put it this way: when you heat water in a kettle, some of those molecules will appear as vapor, but you can't tell in advance which molecules will.

This whole approach is now permeating biology and medicine. René Dubos, of the Rockefeller Institute, said that we cannot say that the tubercle bacillus is *the* cause for tuberculosis. The reactions of the host are even more important. Some of this is old hat, I will agree, but I want to emphasize that we have to look for a number of features, a number of factors, in all these illnesses. We get a group of etiological items rather than a cause.

I think with this in mind we can say that a psychiatrist approaches these illnesses in a comprehensive way. He emphasizes that in addition to the inspective analysis of the data, we must have an introspective analysis of the data. This takes into account the inner life of the patient, his feelings, fantasies, attitudes, modes of thinking, his fears, hopes, and conflicting motivations.

In addition he, of course, takes into account the data obtained by the modifications of the lens, clock, and yardstick, such as physical examination, x-ray, stool examination, gastroscopic analysis, and pepsinogen levels of the blood, or what you will, so that we must use both these means of analysis, an introspective analysis as well as an inspective one. This is necessary both in formulating one's diagnosis and in planning one's mode of treatment. It is particularly necessary in devising experiments, in doing research, and in its still more sophisticated usage in psychosomatic medicine.

The work of Walter B. Cannon, the famous physiologist, has, of course been of primary significance in this matter. His research was rather more teleologic than causal. We are certainly a long way from establishing proved causal relationships, even in the sense of multiplicity of causal elements, between inspective and introspective data. We are in the infancy of psychophysiologic medicine. I think nevertheless a beginning has been made and, most important of all, many leads for further research have been established.

I think this combined and comprehensive approach to the patient leads directly to a consideration of the patient in his environment, since his inner life,

or intrapsychic processes, are a result of learning, and that learning is based on past experiences with others. The physician then must turn his attention to the ways in which his patient interacts with the significant others in his life, and a knowledge of the transactions of the patient with his family, occupational, and recreational groups, among other groups, is necessary to round out the picture. Hence, social and cultural factors are enormously important in understanding the individual sick person.

I think the upshot of all this is what we call a holistic or perhaps a comprehensive approach to the patient and, by the way a "doctor-psyche" approach is just as erroneous as a "doctor-ulcer" approach. I think it is this frame of reference, seeing the patient transacting with his environment, and seeing his adaptive and not-so-adaptive responses to life stresses, which is the approach that I would encourage.

Dr. Browne:—Thank you, Dr. Lief. Now may we hear from Dr. McGlone?

Dr. Frank B. McGlone:—I appreciate the opportunity to participate in this panel. It is more difficult to discuss functional than organic disease. Since the subject is difficult, it is often neglected.

The definition of "functional" is important. Probably no one definition would satisfy everyone on the panel. I like to think of "functional" as describing a disturbance of a function of the digestive tract, whether it be motor function or secretory function of the gastrointestinal tract. This functional disturbance may or may not be associated with organic disease of the digestive tract.

Gallbladder disease, for example, may cause functional disturbances of the digestive tract, including those symptoms of fullness, gas, and belching, which we feel are due to motility disturbance. Gallbladder disease also can be present, when such functional disturbances are not related to the gallbladder pathology.

Listening to Dr. Lief reminded me of a colleague who, when he is teaching medical students, points out that it is important to be able to tell the patient the cause of his disease. He has found that "virus" is a good answer to a lot of questions that the patient might ask; or, "it's something going round". Many patients seem to accept such simple statements wholeheartedly. If the patient is intelligent, or thinks he is intelligent, he tells them the disorder is psychosomatic. The patient feels he can't ask more questions because he should already know what psychosomatic means. (Laughter)

The etiology of functional disturbances is important to consider for a moment. Many inflammatory lesions of the digestive tract can produce changes or symptoms that we would interpret as being functional, that is, not specifically related to disease. As Dr. Crohn pointed out so well yesterday, many patients with regional ileitis will go for years with disturbances that are considered functional and yet the cause of the symptoms is an organic disease. Certainly,

there are neuromechanisms, endocrine dysfunctions, and irritants of various sorts that can produce functional disturbances.

Such simple situations as absent teeth can often be the source of disturbances of the digestive tract which are in the functional category. Excessive food intake, drinking, or smoking can frequently be the cause of many of the functional disturbances of the digestive tract. Perhaps, in the last analysis, excesses or neglects are psychiatric in origin. Many people who eat too much, however, when placed on a diet will lose their symptoms of dyspepsia. Such patients are not likely to need formal psychiatric help.

Consideration of all the factors which may cause the functional complaint is very important. Many organic diseases of a serious nature can present themselves with functional complaints. Hidden in the midst of the functional complaints that the patient considers most important one may elicit some symptoms, such as bleeding, weight loss, or change in bowel habits, that might be a very important clue to organic disease.

It is embarrassing to tell a patient that his complaints are psychosomatic and then have a colleague call you later and tell you that he saw your psychosomatic patient with metastasis to the liver.

The diagnosis of a psychogenic cause of a functional disturbance of the digestive tract should be just as specific as the implication of any other etiologic factor in functional disorders. Gastroenterologists and physicians should handle patient referrals to the psychiatrist very much like the patient referred to the surgeon. Harm can be done by referring the wrong individual to a psychiatrist just as unnecessary surgery may be harmful. If a patient is in need of psychiatric care, he is done a great service—and the psychiatrist is given an assist if the patient is properly prepared for the visit to the psychiatrist.

The diagnosis of the cause of functional complaints, whether due to poor habits, organic disease, or psychogenic factors, is very important.

Dr. Browne:—Thank you, Dr. McGlone.

Already we have drawn some lines in this discussion, as you have heard.

It now becomes important for us to agree on what functional disturbances are. Just what is included in "functional disturbances". We will see a little later whether the panel agrees.

Dr. McGlone has also brought to the fore the important question of diagnosis, how you make the diagnosis of functional disturbances. He has also touched on therapy. When should you refer these patients to the psychiatrist should they have a psychic or emotional factor involved?

We have Dr. Neefe, who is quite adept at summarizing and let's see what he has to say.

Dr. John R. Neefe:—When Dr. Browne asked me to take part in this panel, I did it with some concern because I am sure, as most of you have felt when confronted with a patient with functional disease, you realize one has a sort of alarm reaction to start with. We realize it is a long and detailed problem and it is going to take a lot of time, and the tendency is to hand out some medicine which helps for a little bit. Then the patient returns, and you change it to something else.

Something I do want to emphasize a little, and which is perhaps back toward the direction of the organic again, is: how do we get for ourselves the security we need to tell people that they have a functional disease?

The problem, as I see it is: how do we get accustomed ourselves, as we see these patients, first of all, to decide for ourselves it is a functional disease. By this I am thinking of one where organic disease is not present. I think, first of all, it requires the confidence of the doctor in himself to begin to treat a patient of this sort.

Obviously, in order to have confidence with such a patient, I have to prove to myself that he doesn't have some organic cause. Granted, sometimes both exist—quite frequently both exist. There are a number of elusive conditions which people have that cause what we assume to be functional symptoms.

I just jotted down a few things which have impressed me in recent years. First, there is the difficulty in diagnosing some inorganic diseases. There are several rather nebulous ones. We have all heard of the so-called abdominal angina. It is a very hard thing to diagnose, yet I think it is possible that that condition may exist and may cause recurrent abdominal pain.

There has been a lot of emphasis—Dr. Alvarez has written frequently about it in his column lately—on so-called abdominal epilepsy. I think sometimes even we physicians have difficulty in visualizing how these conditions do produce symptoms. I hope that Dr. Lief might be able to elucidate this somewhat for us. This, however, takes us back to the cerebrum or other parts of the brain and may suggest how some intraabdominal symptoms may arise from that organ.

We have to admit the existence of diagnostic failures. There are x-ray men and x-rays, and still some miss something. We have studies and restudies for obvious organic lesions. These occur sometimes only intermittently and you study them at one time and find nothing, and the next time, if you happen to get the case at the right time, you may find intermittent intussusception or recurrent volvulus.

Porphyrinuria is not a common disease yet the number of cases which occur is surprising. One may, during an asymptomatic phase find nothing, but if you study it at the correct time, you may make a diagnosis.

I recall very well one patient with severe abdominal pain who truly needed a psychiatrist because he had been to so many doctors that he feared he actually had no disease. Literally, he had become an extreme mental case. All the studies were negative but we finally operated upon him. Dr. Ravdin operated, and he had a very tight band between the peritoneum and the liver, which no x-ray study nor any other diagnostic study would ever show. Thereafter he had no pain; one of my most grateful patients.

Amebiasis is easily overlooked, as are some of the collagen diseases. I merely mention these to keep ourselves alert so that we do not make the diagnosis of functional disease too easily, just because a person has had two or three conventional negative diagnostic studies.

Dr. Browne:—I feel we have drawn the lines pretty well and got a fairly good cross-section of thinking and attitude of these men. I believe we should have a little clearer definition of what we mean by "functional disturbances". What is the definition, Dr. McGlone?

Dr. McGlone:—I thought I gave my definition.

Dr. Browne:—Dr. Bargen, what is your definition of "functional disturbance"?

Dr. Bargen:—In general I agree with Dr. McGlone. We speak of disturbed function of an organ or an organ system, both due to organic disease as well as due to emotional and other types of disturbances. I believe that the problem referred to on this occasion is disturbances which occur without evidence of any organic basis, and my definition then would be: a disturbance of the digestive tract or some portion of it, unrelated to organic disease.

Dr. Browne:—Dr. Lief, do you agree with that definition?

Dr. Lief:—In order to have some fun around here, I will say most assuredly I do not.

Dr. Browne:—I thought so.

Dr. Lief:—The term "functional" is one of my particular *bête noires*, I think. I don't know how many of you came across an article in the *Journal of Medical Education* a couple of years back. Apparently one of the senior medical students, I think, at one of the midwestern schools asked his fellow classmates to give him a definition of "functional", and he got about 23 different definitions of the term. He did the same thing with the faculty and got precisely the same result.

It is one of these words which is extremely confusing. I cannot for the life of me see how you can have any functional disturbance without structural disturbance. It might not be demonstrable with our methods of investigation at

this point, but at least at the cellular or perhaps the molecular level, you do have structural changes, so I think the term is extremely misleading.

I think if we define it in such a way so that we all can agree on an operative definition here this afternoon, we can continue to use it, and perhaps that is what we ought to do. But, certainly, the term "functional" as used to mean "idiopathic", or "of unknown etiology", or the definition Dr. Bargen and Dr. McGlone have given it, a disturbance of physiology without any demonstrable organic or structural change, makes no sense to me. It has meant so many things that I think we do have to define the term carefully.

Dr. Browne:—Well, that is not so far apart as I had anticipated, and I was very glad he didn't get further into the actual cause of disease. The truth is we know so little about the actual cause of disease. We know some of the things that occur in a given cell but why and how it occurs is by no means clear at present.

Dr. Neefe:—I would say that I would probably be in agreement with both of my predecessors. I think it is purely a matter of interpretation. My own concept is that every functional disease must be thought of in terms of something working or not working, so I think as we use it in terms of disease, we think of abnormal function.

I don't see how anyone can dispute the possibility of some intracellular change which might be present. But I believe that if we think of this in terms of the condition in which no demonstrable structural disease is present, at the present time, we might have something that we could lean on until we learn more about this.

Dr. Browne:—Then I think the panel can agree to confine their discussions and interpretations to that point, which seems to be the majority, at least we agree there is a disturbance of the normal physiologic function without demonstrable organic disease at certain levels.

Dr. Lief:—May I respond to that?

Dr. Browne:—Surely.

Dr. Lief:—If we make that definition here (I will be the devil's advocate), this will exclude such items as peptic ulcer and ulcerative colitis from the discussion this afternoon, that is if we stick to the title of the symposium, "Functional Diseases of the Gastrointestinal Tract".

Dr. Browne:—Well, I feel there still remains a question, and I hope in our further discussion of this we are going to bring it in. The question, whether functional disturbances, as you have just heard, will ultimately develop organic disease, will be further clarified in answering a number of questions which have been sent in.

I think right now we had better decide what parts of the gastrointestinal tract we will discuss, the tract in its entirety or what parts should we include in our discussion this afternoon.

Dr. McGlone, where do you think we should start and do you think there should be any exclusion?

Dr. McGlone:—There are several organs that should be excluded from this discussion. The organ systems which are most frequently involved, such as the biliary tract and the colon, should be discussed. Perhaps, the stomach and pancreas could be included if time permits.

Dr. Bargen:—I would add the esophagus. We should include the intestine.

Dr. Browne:—You would exclude the small bowel unless we have questions related to it.

Dr. Neefe, do you have any ideas as to what we should continue to discuss or exclude?

Dr. Neefe:—I don't believe we have very much left here, and I think maybe the Moderator might pick one of them out and start off.

Dr. Browne:—Dr. Lief, do you have anything to say?

Dr. Lief:—No, I don't seriously propose that we leave out peptic ulcer and ulcerative colitis. If we leave those out, we won't have too much to talk about, I am afraid, so I really think we ought to include them, I just wanted to bring out the point that the definition of "functional" which we have made is still misleading.

Dr. Browne:—Then we are going to include the entire gastrointestinal tract, starting from the esophagus and, should time permit, include the bile duct.

We have agreed there is certainly an emotional factor in these cases and some involvement in the autonomic nerve mechanism in the production of the symptoms. This has been, I think, intimated by most of you, and we should find out, then, how some of these symptoms might be produced and through what pathways they are mediated.

Dr. Lief, will you talk to us a little about this?

Dr. Lief:—You are asking where the symptom is produced?

Dr. Browne:—Yes. You get the pain and other disturbances are produced. Through what pathways are they mediated? Does it involve all of the autonomic, sympathetic and parasympathetic systems?

Dr. Lief:—I suppose if we start with pain, to look at it from two points of view, in most situations, of course, there must be some local stimulation of the

nerves, let's say the enteric plexuses in the bowel, and this is what produces pain. The stimuli may be a variety of things. We don't know for sure whether, for example, it is hypersecretion in peptic ulcer which serves as the irritant, or whether there are some other factors which become the active stimuli.

I think theoretically one can say one can have pain, even in the absence of local irritation. We know that perception occurs in the highest levels of the nervous system in the cerebral cortex and it is quite possible, for example, to have some kind of disturbance, whether it is a specific lesion, or some physiological or biochemical disturbance in the cortex which can produce pain even in the absence of local factors.

Well, maybe that is enough to get it rolling.

Dr. Browne:—Dr. Bargen, do you feel that these symptoms are mediated through, we will say, the parasympathetics? Why is it, then, that certain organs may be involved and others not, with the same stimulus? Is there any proof that there are certain fibers, we will say, of the vagus activated under a given stimulus, while other fibers are not involved?

Dr. Bargen:—I presume we are discussing pain and distention, diarrhea, constipation, and all the other complaints that patients with functional disorders have. I am not sure that even though we refer them to a particular organ, they actually are of that organ, but we do know that periodic spasm—I never thought that was a very good word, but it is the only word I know to describe what I am thinking about,—of the intestinal tract results in a pain stimulus.

Now, those spasms can occur almost anywhere in the intestinal tract, and they often occur without any demonstrable change, at least any change that we can demonstrate by any means at our disposal at this time. Now, if they occur in the upper intestinal tract, I presume they are mediated through the vagus nerves.

Dr. Browne:—We know, then, that in peptic ulcer we will have the vagus nerve involved to increase the secretory function of the stomach. Is that brought about by a selective action on a certain group of fibers in this nerve, Dr. Lief?

Dr. Lief:—Well, I don't think I can answer that specifically. What we do seem to know is that parasympathetic fibers are not discharged simultaneously all over the body, that we can find evidences of parasympathetic overactivity at one point in the bowel and a short distance away no evidence of such overactivity; likewise, when you use anticholinergics such as Banthine, Dactil, and so forth, you can find evidence of response in one part of the gastrointestinal tract and not in another. Likewise, although it does occasionally occur, it is still very rare to find a patient with both peptic ulcer and ulcerative colitis appearing together, so it looks as if we do not get massive discharge, but more or less selective discharge of, say, the parasympathetics.

Why particular regions of the gastrointestinal tract are selected, is beyond me, and so far as I know, I don't know anyone who knows the reason for it.

This brings us into the general area of specificity of these responses. I don't know, Dr. Browne, whether you want to take that up right at this point or wait.

Dr. Browne:—Well, we might pass now from this question of why one individual, under emotional stress, will develop chronic ulcerative colitis, and the same individual, say 40 years later, develops peptic ulcer.

Dr. Lief:—In general, why does the patient get peptic ulcer rather than ulcerative colitis, or why does he get cardiospasm?

Our research into specificity is really only in the beginning. I might tell you an interesting experiment going on for some years at the Institute for Psychoanalysis in Chicago. They set up a team of seven people, and what they did was to take patients with known illness, such as ulcer, or hypertension, or ulcerative colitis, or rheumatoid arthritis. I think they usually use seven different diseases.

They would interview the patients pretty exhaustively in perhaps one or two interviews lasting at least an hour and a half apiece, and then delete any reference to the physical side of the illness. Then they would present this material to the panel and ask them whether they could identify the particular illness; in other words, it was an attempt to see whether personality patterns or specific emotional conflicts could lead one to be specific about the type of illness which the patient had. Although the results were somewhat encouraging we have a long way to go to determine the factors which are responsible for the specificity.

We have to investigate genetic factors. These have been largely neglected up until the present. We have to investigate such things as conditioning experiences early in childhood. This type of research still has to be done.

Dr. Browne:—I think we should now move to some specific disturbances in organs of the gastrointestinal tract.

Dr. McGlone, would you say a word about disturbances of the esophagus which have been referred to as functional, such as *globus hystericus*, Plummer-Vinson's syndrome?

Dr. McGlone:—*Globus hystericus* is a condition one might put in the psychogenic category, as well as the disorders that might be considered in the realm of conversion hysteria. One cannot find or demonstrate any actual physiological disturbance in *globus hystericus*. No physiological or pathological abnormalities are noted in other hysterical difficulties in swallowing.

The Plummer-Vinson syndrome, on the other hand, is one which can present itself with the complaint of dysphagia. There is, however, in this condition

definite pathology and disturbed physiology of the esophagus which produces definite disturbances in swallowing.

Cardiospasm, which is seen quite frequently, is definitely a disorder of motor function.

Studies on cardiospasm have led to clarification and confusion as to the innervation of the esophagus. The esophagus in different disorders behaves differently. Response to drugs is not consistent. The anticholinergic drugs, which would be expected to relieve spasm, often make a spastic disorder or other motility disorders of the esophagus worse. The innervation of the esophagus is both sympathetic and parasympathetic and the responses are different. Different drugs can produce reactions via the parasympathetics or via the sympathetics and different patients respond differently.

With dyssynergy of the esophagus there is no spasm of the cardia. A dilator may be passed through the cardia with little resistance. On the other hand, there is tone to the cardia and lack of tone to the area above the cardia. Dilatation of the cardia, by reducing the tone of the cardia, prevents the normal resistance of the cardia. Food will then pass through the cardia, despite the lack of esophageal tone.

Globus hystericus, like hysterical vomiting or other conversion hysterias, should be treated by the psychiatrist. Cardiospasm, on the other hand, is more adequately handled by the gastroenterologist with the use of drugs, dilatation, or other needed therapeutic methods.

Dr. Browne:—Dr. Bargen, years ago you did considerable work on this problem.

Dr. Bargen:—I think Dr. McGlone covered the subject very well. Functional vomiting and *globus hystericus* as a group of symptoms are all very similar, and probably they in some way are manifestations of the "conversion syndrome".

Dr. Browne:—You stated a while ago that functional disturbances on a psychosomatic basis did not ultimately wind up in organic disease. Now we have organic changes taking place in the esophagus, as in cardiospasm, ultimately developing a stockingfoot esophagus, and so forth. Does that make any sense to you?

Dr. Bargen:—There is probably some change in the innervation of the esophagus though we don't actually see disease on the mucosal side. There isn't much question that changes do occur, but they are not the result of the *globus;* they are the result of the vomiting, and we do see them in erosive esophagitis from continued vomiting. I don't quite see the relation between the problem of cardiospasm and the problem of *globus hystericus.*

Dr. McGlone:—May I interrupt and point out that I feel, Dr. Bargen, that *globus hystericus* is a purely psychogenic disorder not accompanied by sequela.

Cardiospasm is probably not psychogenic in origin, rather it is an anatomical physiologic disorder.

Dr. Browne:—Dr. Lief, do you agree with that?

Dr. Lief:—As usual, no. I think that cardiospasm like any of the other entities, is not purely psychogenic or somatogenic. Referring to the original discussion of causality, I would say there have to be a number of factors present.

I see John McMahon in the audience, who has written quite a good deal about cardiospasm. I am sure he could answer this a good deal better than I can, but it certainly is my impression that psychogenic factors play a role in the onset of the illness, as well as in succeeding "attacks", and I would say in general that is what I find for peptic ulcer and ulcerative colitis as well.

We get into difficulty when we start talking about causes. That is why I led off with that introductory statement, I think if we approach these things by looking at various hereditary phenomena, and then look for the particular somatic features which must be present for an illness to occur, it tends to be helpful.

For example, in peptic ulcer we have to have, I would think, gastric hypersecretion, say with a high level of pepsinogen, and we also would have to have a particular emotional conflict, and then—which we don't need to go into at this moment—at the time that the peptic ulcer occurs, some stress from the environment which really increases this emotional conflict very markedly. So you have to have a number of factors present. Hypersecretion by itself is insufficient.

It has been shown that in between the bouts of ulcer, with the ulcer healed, many patients still continue to have very high levels of acid secretion in the stomach so that in itself is insufficient to produce the ulcer. Now, these people, however, when presented with a threat to their security or loss of a love object, a threat to their dependency relationships, then they generally develop ulceration.

Dr. Browne:—Our time is moving on. It probably would be well for us to discuss the stomach. The one entity which has stimulated more investigation, and probably much controversy, is peptic ulceration.

Dr. Neefe, would you like to talk about peptic ulcers with relation to psychosomatic factors, or the organic feature; what relation does the psyche bear, if any?

Dr. Neefe:—I think, again, that this is one problem to which you get several different answers, but at least personally it is hard for me to escape the conviction that the psyche has something important to do with peptic ulceration. We see, for example, patients who may be involved in some traumatic experience who will immediately have a hemorrhage from an ulcer within the next few days.

Of course, the old familiar ulcer after a burn is well known. Now, whether you can call that truly of psychogenic origin is a question. There may be many other factors tied up in the whole problem, which I suspect is the truth of the matter. One of these things may initiate a physical factor which may include hormonal as well as the sympathetic, and parasympathetic imbalance, and hypersecretion, and hypermotility.

Perhaps we must also think about the person involved. There are some people who never get ulcers in spite of all sorts of stress. That is something we have all thought about. Heredity may govern to a large extent, not only whether these people get these conditions, but also perhaps the organ involved. We may take, for example, the occurrence of peptic ulceration in a person using steroid therapy. In people who require that, it can be noted that frequently they have certain personality characteristics but at the same time may not have developed ulceration until some hormonal factor comes along which influences the picture. Just exactly what that change is I don't particularly know. My own feeling is that it is going to be difficult to isolate one factor from another. Perhaps the important thing is what initiates it, and I think then we have several other things that come into play.

Dr. Browne:—Dr. Bargen, what is your opinion of the relationship of ulceration and the emotions?

Dr. Bargen:—Dr. Neefe has discussed a number of possible factors in the etiology of peptic ulcer. Emotional disturbances represent major factors in increasing gastric secretion. Some ulcers are mere mucosal erosion, and some are deep, penetrating ulcers. It would seem that more than a nerve-mediated mechanism is required.

Excessive secretion and excessive motility are factors in keeping ulcers active. Whether they are the major factors in producing them is uncertain. The average peptic ulcer is a duodenal ulcer and appears in the first portion of the duodenum, and I think it is very reasonable to assume that excess pouring of acid secretion into that person's duodenum is causative. Nervous mechanisms play a part in the production of excessive gastric secretions because the ulcers are likely to occur in an individual at the time of a marked state of tension, emotional shock, and other phenomena which are mediated through the nervous system so there seems little doubt that the inception, progression, and continuation of the ulcer is aided and abetted by emotional disturbance.

Dr. Browne:—There is a certain inherent quality or predisposition of the individual, the X factor, that protects gastric or duodenal mucosa against ulceration during periods of distress or trauma that might come. Is that what you had in mind?

Dr. Bargen:—I think so.

Dr. Lief:—May I reply to that?

There is some evidence, for example, the Mirsky study—he discovered that 12 per cent of infants had pepsinogen levels in the range of the adult ulcer patients and 0.5 per cent of such infants had levels of pepsinogen that were above the mean of the adult ulcer patients, so that you find a range of pepsinogen levels in infants at birth, and some of them are apparently hypersecretors right from the start.

It brings up the interesting point made by Mirsky that some of these infants may never be sufficiently nourished by their mothers; that no matter how much food they are given, they are still hungry. So, we have not the picture of the rejecting mother but of the rejecting infant. In this situation the mother may respond with guilt and anger to the infant, and further reject the child, setting up a vicious circle in which the infant feels rejected over and over again. Whether this particular vicious circle then becomes a conditioning response for the infant later on in life is still speculative, but these are interesting observations and speculations.

Dr. Browne:—Dr. Neefe, did I see you scribbling notes? Let's hear what you have to say.

Dr. Neefe:—I wanted to ask Dr. Lief why it is some people will go through a very stressful period of extreme anxiety and worry, and feel fine, and all of a sudden their problem disappears, and perhaps happily so, and a week or two later they will turn up with an ulcer, when seemingly their distress has been relieved?

Dr. Lief:—It sounds like a loaded question. (Laughter)

I am thinking whether I have seen a patient just like that, and, offhand, I don't remember seeing one like that, but I am sure it can occur.

I think that we have to look at it from two points of view, speculatively. One is the time factor, that is, the stress, even though relieved, may have been producing pathological effects which turn up, after the stress is over. Secondly, there are many people who do very well under certain types of stress but not so well when they are successful. Success itself becomes a stress for these individuals. We call these people "flushed with success". That is a phrase we use to describe those people who become very guilty about their successful handling of a situation.

Over and over again we see individuals who, just at the peak, or just at the point of a success, whether it is academic work, or on a job, come down either with depression or some type of physical response as a result of "guilty fear". In these individuals, success is unconsciously equated with murdering their competitors.

Dr. Browne:—Dr. McGlone, do you have any other comments, or do you agree with what they have said with respect to peptic ulcer? The question here

is why at one time a gastric ulcer, and another time a duodenal ulcer under similar distress; why do they respond differently?

Dr. McGlone:—That is probably a question to give to the psychiatrist. Psychiatrists always have an answer for everything (laughter) but it isn't always practical. (Laughter)

Now, it has been pointed out that a patient may get an ulcer during a period of stress (pleasant or unpleasant). We are all exposed to tense situations daily. These problems are typical of those referred to by Dr. Bargen in relation to peptic ulcer. One can't drive across town without having some tension or stress, and the patients with peptic ulcer are no exceptions.

As I mentioned in an earlier discussion, if similar lesions occur in the skin, or if someone gets recurrent herpes, nobody gets disturbed about the psychogenic etiology. Recurrent herpes of the mouth is similar in many ways to peptic ulcer. Some people get herpes on the lips and never get it inside the mouth. Others get herpes in the mouth and never on the lips. We don't worry about the psychogenic aspects of herpes but treat these lesions symptomatically with each recurrence. The answer is, we don't know why ulcers originate in the stomach or duodenum. Since we don't know, let's not assume that the cause is psychiatric. Let us, as physicians, evaluate the significance of the stress in our ulcer patients and treat each facet of the ulcer problem individually.

Patients with peptic ulcer or ulcerative colitis are examples of individuals who make very satisfactory patients. Physicians should be able to handle the psychic problems in 90 per cent of the stressful situations in their patients. Once in a while a serious mental problem is encountered and the aid of a psychiatrist is necessary. Proper utilization of the psychiatrist enables the patient to benefit from his service and enables the psychiatrist to do a good job.

Dr. Browne:—He is anxious to answer that!

We have a question just handed in, and for a moment I would like to turn to the matter of hormones. This question asks whether the stress factors and adrenocortical hormones play an important role in the peptic ulcer problem.

Dr. Neefe, do you have any comments on this?

Dr. Neefe:—I think the only thing that I can say from personal experience, from having used a good many of the steroids, primarily in certain types of liver disease and some other things, is that it is a really hazardous problem, the complication of ulcer in any of these patients who have had long-term therapy, and I think it is much more than a coincidence.

Dr. Gray, in Boston, and others, of course, have done many studies on the effects of steroid therapy on gastric function and, as I am sure most of you know, regularly show increases of pepsin activity in the urine. The question

then arises as to whether uropepsin really has to do with ulcer. This happens only in the ulcer-predisposed patients. It is a thing we don't know about, but it certainly does happen, and the same thing with butazolidin. It is a factor, but I think it develops into one of several things.

Dr. Browne:—Dr. Bargen, you have followed a lot of gastrectomies. When the patient with an established achlorhydria is given adrenocortical hormones the uropepsin is positive, or increased. Is this correct? Would you comment on it.

Dr. Bargen:—I have no experience with using steroids in that type of case. I am in agreement with Dr. Neefe about the cautious use of steroids in all these people because of the risks involved. I use steroids for all types of digestive disorders in rather limited amounts.

Dr. Browne:—Our time is getting so short. I will move now to another controversial entity, and there are a number of questions dealing with it.

It has been stated here that chronic ulcerative colitis, irritable colon, unstable colon, are purely psychosomatic in origin. Dr. Bargen, how do you feel about this?

Dr. Bargen:—How much time do we have?

Dr. Browne:—I will give you five minutes.

Dr. Bargen:—The various conditions you have mentioned are of two entirely different groups of digestive disorders. Chronic ulcerative colitis is not of psychosomatic origin and if you treat it as if it were, you will go wrong more often than you will go right. The reason for that opinion is simply this: most of you in the audience, I assume, are internists or gastroenterologists. I don't know how many psychiatrists are sitting before me. I am sure most of these patients are treated by the internist. There are a few mentioned by Dr. McGlone, perhaps 10 per cent,—and in my experience even less—who present emotional problems. They are so emotionally upset that a psychiatrist is called in consultation and so the psychiatrist has arrived at the conclusion that the 10 or less per cent represent ulcerative colitis patients as a whole.

People with ulcerative colitis are ordinary people. They come from all over the country and many parts of the world, and they are usually normal, but sick, individuals. When they become asymptomatic, all nervous symptoms and emotional disturbances be they ever so many, disappear, or, if colectomy becomes necessary to do away with the disease, they become very ordinary individuals.

These facts speak against the disease being of psychosomatic origin.

Vomiting and diarrhea commonly mirror disturbances of the digestive tract. They are common symptoms of the disturbed digestive tract. The patient may vomit and have diarrhea because he is emotionally upset and it is considered a

possible step to the development of inflammatory organic change. Wolf and Wolff showed that under psychiatric stimulation, an individual might develop hyperemia and edema of an exposed colonic mucosa but when the psychic stimulus was removed, the mucous membrane returned to normal, so that the step from the irritable bowel, or the functional disturbance, to the actual organic change has never been completed. I have only seen an occasional individual who had a functional disturbance of the bowel for a long time develop ulcerative colitis later.

Dr. Browne:—That leaves no question as to his thinking, as I understand it, and this leads to our next question.

Dr. Lief, will you answer this question: Can you establish a personality pattern that will tell us whether an individual will develop a chronic ulcerative colitis or a peptic ulcer?

Dr. Lief:—Well, this is rather a difficult question to answer without taking a lot of time to go into the ramifications of it. It is very difficult to give generalizations which can be applied universally. It is a situation in which there are many steps.

First of all, we are getting away from trying to ascribe a specific personality pattern to a specific illness or illnesses. Research has tended to bring out that there are specific conflicts which are related to specific illnesses. For example, in peptic ulcer a group of psychologists working in an army center, working blind with psychological testing, was able to select 85 per cent of hypersecreted individuals, just on the basis of psychological tests. It indicates that there is something there which can be picked up.

I would say in general, in answer to the question of differentiation, that people who develop peptic ulcer and those who develop ulcerative colitis—mindful, of course, of the many exceptions—that people who develop peptic ulcer tend to have a very pronounced conflict over intense needs, to be taken care of, to be fed symbolically. These are people who deny this particular need either because it produces shame or humiliation, or because external factors make it necessary. On the other hand, people who develop ulcerative colitis, in my experience, tend to be very compulsive people, people who tend to internalize their angry feelings and respond with depression to loss of love objects, or job, or anything else which threatens their security or self-esteem.

Now, it must be borne in mind that there are plenty of such people who do not develop ulcerative colitis. Well, I am stressing the fact that there have to be psychological features in conjunction with certain unknown somatic features, let's say in ulcerative colitis, before one sees the final picture of the disease.

Dr. Browne:—That seems to be a very practical approach, and brings it back to Alexander's attitude years ago. This next question I think will be of

interest to all of us: "How do you make a diagnosis"? We would like to know how you would make a diagnosis of functional disturbances of the gastrointestinal tract.

Dr. McGlone, how do you examine these patients? What do you do to make a diagnosis?

Dr. McGlone:—The diagnosis is made just as in any other disease, on the basis of evidence that supports the diagnosis.

It impresses me, particularly in the older individuals, that it is important to do a very thorough examination. We have recently been doing some examinations for companies where they want a thorough examination of patients regardless of symptoms. We found, as many others have found, that from 50 years of age on, x-ray and laboratory data provide much more unexpected information than in people below the age of 50. In general, a history and a very good physical examination in younger individuals will frequently provide the diagnosis, especially if all factors including the personality evaluation are considered.

Physicians should evaluate the emotional factors well enough to know when the patient needs referral to the psychiatrist, just as they do before referring a patient to surgery.

Dr. Bargen:—I think what Dr. McGlone has said pretty well covers my thinking.

Dr. Neefe:—I have little to add to what Dr. McGlone has said other than that I am sure you all have the same feeling and experience. One of the first conclusions you get when you take the history of patients—they tell you, "I have had these same symptoms for 30 years and I don't really think I am any worse than I was, but this bothers me a lot."

It starts you off immediately thinking about the possibility of—well, I don't know whether we have decided on a term here—functional disease. We use it for what it means, but even in those cases, as Dr. McGlone has emphasized, it has to be proved that you don't have some other factor, because sometimes it isn't just the one thing but some other contributory minor ailment that at least aggravates the whole problem—so many times something worthwhile is found even though it may not be serious.

Dr. Lief:—Well, first of all, Dr. McGlone spoke about most doctors being able to handle these patients, and, despite his needle—I will ignore that, and agree with him. I think most doctors can handle most of these patients, and I think it is an error to refer them, or to try to refer the vast majority of them to the psychiatrist.

I think the referrals have to be done very carefully, and they have to be selected carefully. There is one point, for example, that might be emphasized.

When a patient is in an acute phase of an illness, whether it be ulcerative colitis or peptic ulcer, for example, it is wrong to start probing for psychological features. I think at that time the most important fact is the establishment of a relationship with the patient. The doctor has to set this up first. If he establishes a warm empathic relationship with the patient, and the patient has trust and confidence in the doctor, who becomes then a substitute for someone else in the environment, someone who is significant to the patient in terms of his needs to be taken care of—that is the essential thing. After the acute phase has quieted down, at that time the doctor bit by bit can explore the social and environmental and interpersonal features which may be important, in some cases extremely important, in the management of the disease.

A practical point: for example, it is much better to spend 10, or 15, or 20 minutes with an acutely ill patient on the ward, three times a day, than to sit down with him for an hour, or an hour and a half once every two days.

Dr. Browne:—It certainly seems, then, that in the examination of these patients we should not overlook organic disease. There may be some of us who can make a diagnosis on positive evidence without the aid of other armamentarium; yet, too frequently, and particularly as Dr. McGlone has said beyond 50 there are many unsuspected entities justifying a careful examination of these patients for organic disease. They should not be immediately classed as purely functional or emotional without due consideration of other possibilities. Many things can disturb the function of these organs besides psychic factors.

Dr. McGlone, here is a question for you. Discuss Plummer-Vinson syndrome without a web, and why cases with a web are not relieved by excision.

Dr. McGlone:—Plummer-Vinson syndrome does not usually have a web. Many people feel that this disease does not exist. Others believe that a web may simply result from scarring associated with atrophy or repeated erosions. Usually webs or other evidences of scarring will respond to dilatation.

Dr. Browne:—Dr. Neefe, are duodenal ulcers more frequent in heavy spice-eating populations than in populations taking relatively bland diets?

Dr. Neefe:—That is a very hard question for me to answer because I don't believe I know of any studies that have been made on that particular point. I suppose some of the heaviest spice-eaters might be amongst the Italian population, and I am not aware of any statistics of ulcers in these being more frequent, but I wouldn't want to be an authority on that.

Does anyone else know?

Dr. Browne:—This question had Dr. Neefe's name on it, and the same question was asked of Dr. McGlone. Dr. McGlone, what is your comment?

Dr. McGlone:—I have no information showing that most condiments produce much irritation.

Dr. Browne:—There was a survey once made in Mexico, where they are supposed to eat a lot of chili and "hot stuff". The survey in a small community did not show a greater percentage of peptic ulcers than we have here.

Dr. Bargen, I handed you a question addressed to you.

Dr. Bargen:—"Are the 'functional' diarrheas more frequent in populations using spice cookery, or is there a gradual acclimatization to these stimuli?"

I think there are other reasons for the frequency of diarrheas among those using highly seasoned foods. For instance, across the border people use spices much more freely than we do, but they also have more bacillary dysentery and more amebic dysentery. I am not sure that the spices themselves are the main cause of their disturbed digestion.

Dr. Browne:—It has been said that certain spices cause gastric hypersecretion.

Dr. Bargen:—I think that is pretty definite.

Dr. Browne:—And that is not all spices, but certain spices—cloves, pepper, and paprika, I believe those are the three.

Here is another, a little loaded, for you.

Dr. Bargen:—"Since you do not feel that chronic ulcerative colitis is psychosomatic in origin, do you have an opinion as the probable cause of the disease?"

Well, the first answer is that there are many forms of ulcerative colitis, and I am sure that I am quite incapable of answering that question at this late hour, both as to the exciting factor and the many contributing factors that are necessary in the development of some forms of ulcerative colitis.

Dr. Browne:—That is a nice way out! We have made them say "I don't know" a number of times this afternoon, haven't we? (Laughter)

This is a question for you, Dr. McGlone: How do you "prepare" the patient for psychiatric consultation?

Dr. McGlone:—This answer could take all afternoon. Proper preparation of a patient for psychiatric consultation is important because most patients do not accept the idea of a psychiatric consultation readily. It should be pointed out to the patient that the more orderly, more expert evaluation of the psychiatrist in relation to the emotional and etiological factors of their disease is of primary importance.

It is most important that the physician feels that there is a definite possibility that the patient's disorder is on a psychogenic basis. The illness could be a serious psychogenic disorder and one that is beyond the physician without special training. When the emotional disturbances are such that simple psycho-

therapy, as given by the physician, will not handle the problem the expert help of the trained psychiatrist is necessary for diagnosis and therapy. The patient must be convinced of these points.

Dr. Browne:—In other words, you think that in the preparation of the patient one of the internist's functions is to get the patient to accept psychotherapy. Does that help the psychiatrist at all?

Dr. McGlone:—It helps very much. We have recently added a psychiatrist to our group and find we have a much greater use for the psychiatrist than we did before since we have a much better working unit. He can refer patients back much more freely to us and tell us how to handle them in many instances.

I should like to hear Dr. Lief's comments in relation to these points.

Dr. Lief:—Yes, I think I agree with Dr. McGlone's experience, that perhaps many times consultation with the psychiatrist is unrewarding. I think probably the chief factor in the difficulty is poor communication between the psychiatrist and the referring physician. I think that this is borne out by the fact that when they added a psychiatrist in Dr. McGlone's clinic, where the communications could be handled much more easily and freely, the referrals and consultations turned out to be much more beneficial.

I think that another factor, of course, is selection of patients. Sometimes the internist or gastroenterologist will refer a patient to the psychiatrist, but this patient, although he is very sick, does not have the capacity for insight or uncovering therapy, and the psychiatrist will say, "Well, I can't do very much for this patient. I know he needs help, but the kind of help I can offer will not be utilized by this patient". I think that patient needs supportive or relationship therapy, which can be given by the referring physician and in some instances better than by the psychiatrist.

Dr. Browne:—Dr. Neefe, is the postcholecystectomy syndrome of psychosomatic origin?

Dr. Neefe:—There, again, is a complicated situation and there are a number of causes of postcholecystectomy syndrome. One has to think of two different varieties primarily based on dividing those who have had their gallbladders removed. They will not then be postcholecystectomy but some of these people do have their gallbladders removed eventually for the same symptoms and those patients have not had an obviously diseased gallbladder or a common duct diagnosis.

Patients who have been given a diagnosis or at least have given a history of sluggish gallbladder often have their gallbladders removed, or used to in past years, and following the operation have continued to have symptoms. At least my own impression is that those people probably did not have their symtoms resulting from their gallbladder in the first place, and that either the

correct organic diagnosis was overlooked, or that their symptoms truly were on a psychosomatic basis from the start.

Then you have another group of cases amongst those who have had their gallbladders out and, unfortunately, many of the organic causes are quite difficult to demonstrate. At least until recent years we had no very good way of visualizing the extrahepatic biliary duct system after cholecystectomy, and that is particularly true if considerable liver damage has occurred prior to or following operation. Today many such patients can have their duct visualized either by the intravenous technic or sometimes by the large oral technic, and we find a certain percentage of them will have a retained calculus.

It must be pointed out that even these technics are not 100 per cent reliable because visualization down at the junction of the common duct, with the duodenal structures and ampulla, is often poor or incomplete. A stone can be present there and the duct still look reasonably normal. We think common duct stone is perhaps a formation subsequent to operation and is one of the more frequent causes of the syndrome.

There is quite an interesting number of cases being reported frequently now of dilatation of cystic duct stumps, and in some of those, calculi form.

One interesting cause that I have not seen until recently was that situation in which an actual neuroma was present in the cystic duct stump. The problem of pancreatitis is notoriously difficult to diagnose, and is most common in people who have gallbladder disease, and that always has to be considered.

So our first job is always excluding the natural organic possibilities of this syndrome, and it isn't always easy to do.

I think it is often difficult to get information on this. Fibrosis can occur sometimes from the trauma of probing of the structure during the exploration of the duct, perhaps in association with duodenitis. Quite often, it seems to me, in these very patients one finds, if one looks further or outside this area, the cause of the syndrome.

I am sure that at times it is not organic but, again, there are always widespread opinions on this particular syndrome.

Dr. Browne:—We could spend another hour on this subject, but let us just say to the surgeons, "remove the calculus gallbladder", and give a lot of thought to it afterward.

We have a few remaining questions. Dr. Bargen has a number. I will leave it to his judgment how he handles them.

Dr. Bargen:—"Once ulcerative colitis begins, do emotional disturbances aggravate or perpetuate the disease?"

Very definitely so, just as an emotional upset may result in diarrhea in an otherwise normal person. In a person with ulcerative colitis, the bowel has become a narrow tube, and it is more easily disturbed by emotional reactions. Not only physical, but also emotional rest is a very, very important item in the control of the various ulcerative colidides.

Dr. Browne:—I regret we will not be able to continue, but time has marched on. It has been pleasantly surprising to have the great number of very pertinent questions, and we regret our time will not permit attempting to discuss them.

There is one final question referred to by Dr. Bargen "Does a previous amebic infection predispose to an irritable bowel syndrome?"

The truth is, you have less than 1 per cent of intractable or complicated cases of amebiasis. There is no law against an individual having amebiasis and an irritable colon. I know of no infection in which the results are more satisfactory when properly treated than amebiasis. Most frequently the residual you have results from overtreatment or improper treatment rather than the amebic infection being a predisposing factor in developing the so-called irritable colon syndrome.

I want to thank the panel for their very careful and ample discussion.

LATERAL PORTACAVAL ANASTOMOSIS FOR PORTAL HYPERTENSION*

Long Term Results in 58 Patients with Intrahepatic Portal Bed Block and 7 Patients with Extrahepatic Portal Bed Block

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The type of portacaval shunt best suited for the relief of portal hypertension has been the subject of debate and clinical concern since the turn of the century[1-7]. There are some who are not yet convinced that any shunting procedure has real merit[8-12].

In our experience with 80 patients having portal hypertension, 65 were the subjects of 70 operations for the performance of lateral anastomosis between the portal and caval systems during the past ten years. Twelve of these patients have been previously reported[13]. The majority of the operations were performed by the resident staffs of Detroit Receiving Hospital, Detroit, Mich., the Veterans Administration Hospital, Dearborn, Mich., service of C. G. Johnston, M.D., Children's Hospital, Detroit, Mich., the University Hospital and Veterans Administration Hospital, Birmingham, Ala., service of Champ Lyons, M.D.

Case Material

Etiology:—Liver biopsy was done routinely in all patients at the time of laparotomy. In Figures 1 and 2 are recorded the incidence of intrahepatic and extrahepatic obstruction on the basis of microscopic examination.

Age:—In the cases of intrahepatic block the age range was from 11 to 70 years. In the extrahepatic group age range was from 5 months to 42 years.

Sex:—In the group with intrahepatic obstruction there were 37 white males, 14 white females, and 1 white male child. In the group with extrahepatic ob-

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struction there was 1 white male, 1 white female, 4 white male children, and 1 white female child, and 1 Negro male child (Figs. 3 and 4).

Presenting complaint:—This is documented in Table I. In the group with intrahepatic block, there were 5 patients who presented a problem in accurate diagnosis since melena was the only complaint. In the group with extrahepatic obstruction hematemesis was the only complaint.

Stigmata observed:—The usual stigmata of cirrhosis were frequently seen but not uniformly present. In 19 patients in the group with intrahepatic block

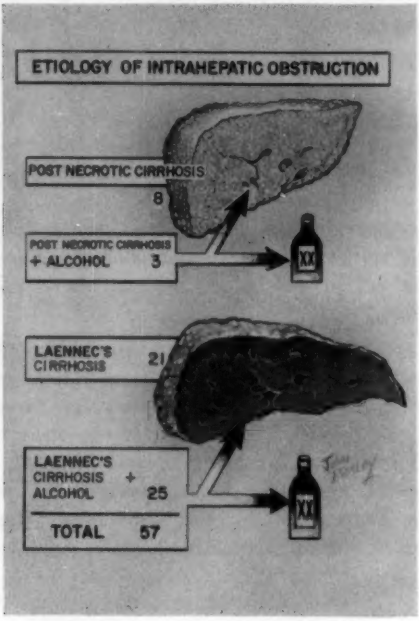

Fig. 1

none of these stigmata were observed and diagnosis was rendered more difficult. In the group with extrahepatic block, splenomegaly[14] was the most frequent indication of the true nature of the underlying difficulty, but in 5 patients diagnosis was obscured by the absence of splenomegaly (Table II).

Other disease states:—There were 3 patients with intrahepatic block who had their treatment complicated by diabetes. No associated disease was observed in patients with extrahepatic block (Table III).

Operations previously performed for control of bleeding varices:—There were a total of 22 operative procedures performed elsewhere in this group of

patients prior to the shunt procedure for control of bleeding esophageal varices. Only the transesophageal ligations were performed by our staff (Table IV). Transesophageal ligation was performed after failure of tamponade as the initial treatment, and only as a means of saving life until a definitive shunt procedure could be performed. One child aged 4, with extrahepatic obstruction entered with recurrent esophageal bleeding after ligation of the left gastric and splenic arteries at age 2. A side-to-side anastomosis between the superior mesenteric vein and the inferior vena cava was performed. Bleeding did not recur until age 5 because of closure of the shunt and she was admitted in shock from hematemesis. Transthoracic transesophageal ligation of varices proved life-saving and the patient has been free of other than minimal bleeding episodes for a period of 10 months. It is currently felt that children under age 10 are preferably treated with transesophageal ligation, repeatedly performed, if neces-

TABLE I

PRESENTING COMPLAINT

Intrahepatic Block	
Hematemesis	27
Hematemesis and Melena	19
Hematemesis, Abdominal pain	6
Hematemesis, Delirium tremens	1
Hematemesis and Coma	1
Melena only	5
Ascites	6
Extrahepatic Block	
Hematemesis	8

sary, to permit the young patient to develop a splenic vein of sufficient size to insure long continued patency of the splenorenal shunt. In adults the transesophageal ligation is an ancillary procedure to prepare a patient for subsequent portacaval shunt under optimal conditions. It is also felt that repeated transesophageal ligations may have a place in the treatment of patients in whom previous portacaval shunts have closed or proven ineffective.

Number of bleeding episodes prior to the shunt procedure:—Six of the patients in this series had never bled. In the group with intrahepatic portal obstruction, there were 27 patients who presented at the time of the first bleeding episode and 10 patients who had bled previously. Although it is uncommon for the patients with intrahepatic obstruction to defer seeking medical assistance at the time of the first hemorrhage, patients with extrahepatic portal obstruction commonly present with a history of previous episodes of bleeding. This discrepancy is usually explained on the basis of the better tolerance of bleeding by the patient with normal liver and may be of diagnostic help in the evaluation of a patient when first seen (Table V).

Diagnosis:—A careful physical examination emphasizes a search for the stigmata of cirrhosis and enlargement of the liver or spleen. Emergency laboratory estimation of the prothrombin time[15], icteric index, and blood ammonia content[17] are done routinely. If jaundice is absent a bromsulfonphthalein test[16] often provides useful additional information. On an elective basis a more complete liver screen is accomplished. Clinical and chemical evidence of liver failure is usually present in the group with intrahepatic block, whereas the absence of these signs suggests that the point of portal obstruction is extrahepatic. Effective esophageal tamponade is the final criterion establishing the diagnosis of bleeding from the region where esophageal varices occur.

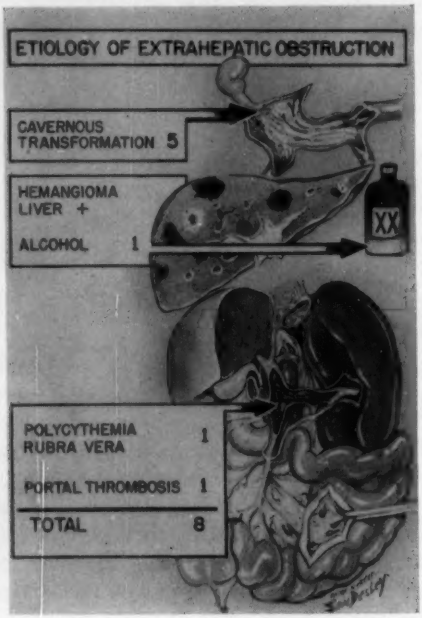

Fig. 2

Emergency measures to control bleeding:—

1. Nonoperative:—In this series we have relied on tamponade for the control of bleeding varices[18] (Table VI). If tamponade is secured and maintained it is of value in localizing the bleeding site to the esophagus, stomach or duodenum. If the bleeding is esophageal in origin, tamponade will usually control it. If the bleeding is from the stomach or the duodenum, the gastric aspirate remains bloody. A pitfall in the accurate evaluation of the bleeding

site is gastric varices, which occur in approximately 2 per cent of these individuals[19,20].

When the varices are located in the stomach, tamponade is not effective in controlling bleeding because of the ability of the stomach to distend and move out ahead of the lower balloon, no matter to what degree it is inflated. Tamponade is not without hazard and a decision must be made in 12 hours whether to persist in tamponade or to consider transesophageal ligation. In "dead-end" cirrhotics the obvious mortality risk usually influences a decision for a further 12 hours of tamponade. The transfusion program should emphasize the use of freshly drawn whole blood in an effort to restore the clotting elements of the blood to normal[21]. If old banked blood is used platelets are deficient and there is a measurable amount of ammonia present[22].

TABLE II

STIGMATA OBSERVED

Some combination or all of the following	Intrahepatic block	Extrahepatic block
Liver palms Jaundice Ascites Splenomegaly Hepatomegaly Peripheral edema Telangiectasia Gynecomastia Testicular atrophy Relative hairlessness	39	3 (Splenomegaly) only
None of above	19	5

If tamponade is continued for more than 24 hours, marked edema and superficial ulceration of the esophagus develop[17,23,24]. If, as a measure of desperation, a surgical attack is contemplated on the esophagus to control bleeding after this period of time, primary healing of the esophagus is rendered less likely because of the protein deficits in the cirrhotic patient with recent blood loss.

2. *Operative:*—If the bleeding is not stopped after 12 to 24 hours of tamponade we routinely perform transthoracic[25,26,27] or transabdominal transesophageal ligation of varices[28,29]. When vascular adhesions are likely to be present as a result of previous operations, we have preferred the transthoracic approach to shorten operative time and diminish blood loss. The transabdominal approach in an unscarred abdomen has the advantage of permitting recognition

of co-existing ulcers and biopsy of the liver. Of 9 transesophageal ligations, all transthoracic, 4 were performed in cirrhotics with 2 deaths and 5 were performed in patients with extrahepatic portal obstruction with no deaths (Table VII).

Preoperative demonstration of varices:—During the period of active hemorrhage, x-ray studies are valueless because the varices are usually collapsed and the clot-filled esophagus frequently leads to confusion. After the bleeding has stopped and the patient is stabilized, x-ray study of the esophagus with barium,

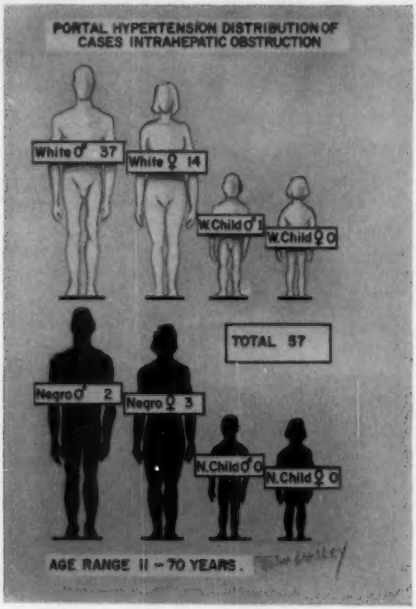

Fig. 3

supplemented, if necessary, with the Valsalva maneuver is the most reliable method for demonstrating varices (Table VIII).

Selection of patients:—We have generally followed Linton's criteria[30] in selection of patients for operation. The blood ammonia level has been of especial help in the postbleeding period for it permits controlled dietary increase in protein without the risk of progressive ammoniemia. An intake of 100 gm. of protein daily without fluctuation in the blood ammonia level usually indicates improvement on medical management alone. A blood ammonia content above 150 gamma per cent is associated with an increased surgical risk. Ascites not responsive to medical management and continuing jaundice are ominous signs

prognosticating a poor postoperative course[31]. In one patient reported herein, with intrahepatic block conservative management for 6 months restored liver function sufficiently to permit a successful shunt and an uninterrupted convalescence.

Operation:—Hunt's hornpipe posture is used in positioning the patient on the operating table and a folded sheet is used to elevate the right side of the body. The right subcostal incision is used and may be extended across the left rectus if necessary. Early in this series a thoracoabdominal incision was used in two patients, but it was found that the thickened fibrotic liver could not be displaced into the chest and there was no advantage in the resulting exposure. Even were it possible to displace the liver, the tension on the structures in the right free border of the gastrohepatic omentum would complicate the performance of a vascular anastomosis and likely result in angulation and torsion of the accomplished suture. Both of the patients with the thoracoabdominal incision complain of thoracic incisional discomfort 5 to 9 years postoperatively.

TABLE III

OTHER DISEASES ASSOCIATED WITH INTRA- AND EXTRAHEPATIC PORTAL BED BLOCK

Delirium tremens	1
Diabetes	3
Gastric ulcer (8 mos. post shunt)	1
Duodenal ulcer (4 mos. post shunt)	1
Hypersplenism	1

The abdomen is explored and portal pressures are measured with a fine polyethylene catheter placed in one of the radicles of the portal system usually a vein in the gastrocolic omentum. After pressures have been recorded portaportagrams are made using the same catheter and while the films are being developed, a liver biopsy is taken. The common duct is identified as well as the hepatic artery and these structures are gently retracted and the portal vein is freed up from the superior border of the pancreas to the hilum of the liver. Following this the inferior vena cava is exposed and using special clamps the portal vein and the inferior vena cava are approximated and a shunt is constructed. This shunt is usually from 10 to 14 mm. in length depending on the cross section diameter of the portal vein. A most important technical maneuver is the removal of an ellipse of tissue from the wall of the inferior vena cava and of the portal vein[32]. The shunt is constructed using the suture technic of Blalock[33] (Fig. 5). Following the performance of the shunt, the clamps are released on the portal side and if there are no leaks, the clamp is removed from the inferior vena cava. It is noticed at this time that most of the troublesome oozing or frank bleeding stops rather abruptly when the clamps are removed and the shunt is opened. Postshunt pressures are then recorded and the abdo-

men is closed with a drain down to but not in contact with the previously constructed shunt.

Portal pressures:—The portal pressures are recorded before and after performance of the shunt. These have been averaged in the group with intrahepatic block and extrahepatic block. In only one case was the pressure higher after shunting than before (Table IX).

Type of shunt performed for intrahepatic obstruction:—In 52 cases the standard lateral portacaval anastomosis was carried out. When there was portal

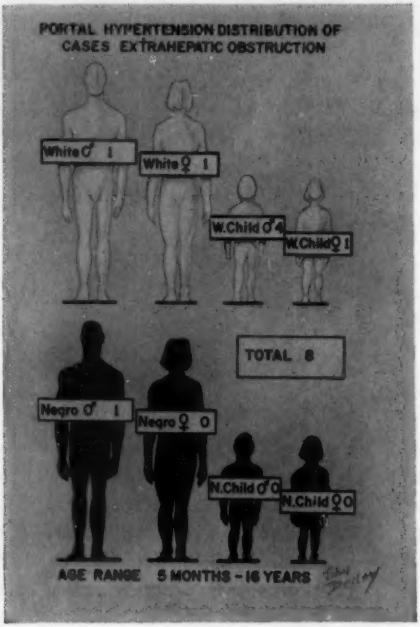

Fig. 4

thrombosis or when there was massive bleeding in the dissection of the portal vein, some variant of the side-to-side anastomosis was carried out. A word should be said about the use of a vein graft when there is caudate lobe hypertrophy. It is unwise to resect this lobe and so sacrifice functioning parenchyma or to accept the risk of bile fistula. An acceptable alternative would seem to be to use the superficial femoral vein as a free graft between the portal vein and the inferior vena cava[34]. This was necessary in only one patient, but this man is doing well with no further episodes of bleeding 14 months after this procedure was performed (Table X).

Type of shunt performed for extrahepatic obstruction:—The splenorenal shunt is the procedure of choice for the physically mature patient. In infants and children under ten years of age persistent patency of the splenorenal shunt is uncommon. In the patients reported here the small children have been treated by lateral anastomosis of the superior mesenteric vein or some other portal collateral to the inferior vena cava. This experience suggests that repeated transesophageal ligations may be preferable to "make-shift" shunts pending the time when the splenic vein is large enough to justify the splenorenal anastomosis (Table XI).

Early operative mortality:—In the group with intrahepatic block there were 11 deaths in the immediate postoperative period (1 to 30 days inclusive). There was only one death that could not be definitely attributed to the underlying liver disease. Three of these 11 patients had postmortem examination. All had shunts which were patent and free of clot. There were no deaths in the group with extrahepatic block (Table XII).

TABLE IV

OPERATIONS PERFORMED FOR CONTROL OF BLEEDING PRIOR TO SHUNT PROCEDURE

1. Splenectomy	5
2. Esophagogastrectomy	1
3. Total gastrectomy	2
4. Transesophageal ligation	9
5. Ligation of hepatic, splenic and left gastric arteries	1
6. Exploratory laparotomy	2
7. Splenorenal shunt	2

Late mortality:—In the intrahepatic group there were 19 patients who expired (41 days to 91 months). Of these only 9 were directly attributable to the underlying liver disease. Of this group there were 8 postmortem examinations performed and 2 of the shunts were closed and six were open and free of clot. There were no late deaths in the group with extrahepatic block (Table XIII).

Hepatic coma:—Hepatica coma is a problem only in patients with cirrhosis. In a previous report we stated that there was a lesser incidence of hepatic coma following lateral portacaval anastomosis in both the immediate and later postoperative periods. The current review of this material fails to substantiate this earlier impression and it must now be regarded as erroneous. There were 8 deaths from coma in the immediate postoperative period and 15 patients who subsequently developed coma. A review of these cases suggests that coma developing in the postoperative period reflects poor selection of patients. Using Ludington's criteria[35] for abnormality of liver function all of the patients operated earlier in this series would probably not be candidates for operation at this time. Of the 15 patients developing coma later, it is certain that 9 continued

to drink heavily and died in coma, without evidence of recurrent esophageal bleeding. The remaining 6 patients in this group abandoned the use of alcohol, responded to treatment for coma, and are living and well at present.

Treatment of hepatic coma:—Restriction of dietary intake of protein is essential for sustained reduction of blood ammonia content[36]. Sterilization of the gastrointestinal tract with neomycin is a useful adjunct if essential vitamins are supplied[37]. Sodium glutamate has proven disappointing and the results with the intravenous use of argenine hydrochloride have been similarly equivocal[38,39]. The blood-filled intestinal tract increases the concentration of blood ammonia.

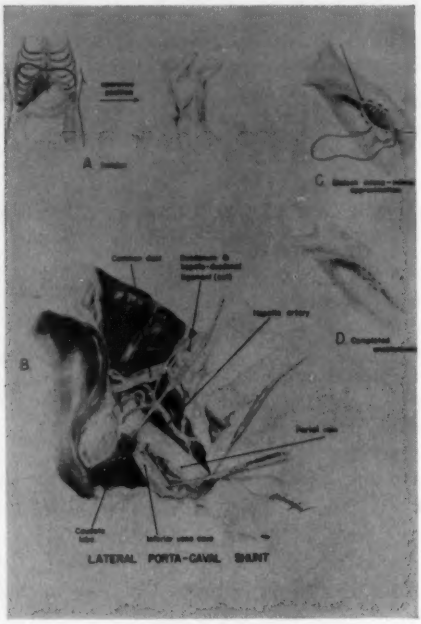

Fig. 5

When this complication is present saline catharsis and intestinal antibiotics are clearly valuable[36].

Survivors:—Of the original group of 65 patients 37 survived. 31 are gainfully employed or going to school. Two patients of the 8 survivors in the extrahepatic group have bled again and two patients of the 29 survivors in the intrahepatic group have had recurrent episodes of bleeding (Table XIV). Both of these cirrhotics with recurrent bleeding also developed hepatic coma. An additional 4 patients for a total of 6 of the 29 surviving cirrhotics also developed

episodes of coma responding to treatment. Two survivors are living and well 9 and 10 years postoperatively (Table XV). It is difficult to conclude that the performance of a shunt actually contributes to survival. This difficulty stems from the fact that patients with markedly abnormal liver functions are excluded

TABLE V

NUMBER OF BLEEDING EPISODES PRIOR TO SHUNT

	None	1	2	3	Many
Intrahepatic Block	6	27	10	6	10
Extrahepatic Block	0	1	0	1	6

from the series selected for operation. There are no statistics available to document the survival of a similar group managed conservatively (Table XVI).

Liver function following the lateral portacaval anastomosis:—There were 14 patients in this series with intrahepatic block who had liver function studies

TABLE VI

TAMPONADE

Effective	42
Ineffective	11

repeated at varying intervals postoperatively. There is no evidence in this group to suggest that there has been marked improvement in liver function. The progress of the basic liver disease has gone inexorably forward. The fact that bleeding is prevented by the shunt may enable the liver to maintain a precarious state of compensation.

TABLE VII

TRANSESOPHAGEAL LIGATIONS

	Number	Lived	Died
Intrahepatic Block	4	2	2
Extrahepatic Block	5	5	0

Peptic ulcer as a complication of lateral anastomosis:—In this series 2 patients of 27 cirrhotics developed gastric ulcers. This compares with Mulligan's recent report[40] of 8 peptic ulcers developing following the performance of an end-to-side anastomosis.

Lateral portacaval shunts for ascites:—Hunt[41] heartily endorses portacaval shunts for the treatment of ascites. Child[42] and Linton[43] do so more guardedly. Three patients with ascites had post necrotic cirrhosis and the other 2 had typical Laennec's cirrhosis. Two of the patients with postnecrotic cirrhosis died

TABLE VIII

PREOPERATIVE DEMONSTRATION OF VARICES

By x-ray	39
By esophagoscopy	3
By operation	8
Varices absent	16

of hepatic coma in the immediate postoperative period, but the remaining patient is living and well without ascites 9¼ years later. Of the 2 patients having Laennec's cirrhosis, one died of unknown cause 18 months postoperatively, and

TABLE IX

PORTAL PRESSURES

	Preshunt	Postshunt
Intrahepatic Block (57)	209-600+ aver. 363	40-440 277
Extrahepatic Block (8)	132-440 aver. 317	110-340 197

the other survived for six years without ascites but died in coma. This experience has not prompted enthusiasm for the performance of a portacaval shunt in the management of ascites uncomplicated by esophageal varices and bleeding.

TABLE X

TYPE SHUNT PERFORMED FOR INTRAHEPATIC OBSTRUCTION

1. Side-to-side, or lateral portacaval	52
2. Veins of Retzius to inferior vena cava	1
3. Umbilical vein to inferior vena cava	1
4. Side superior mesenteric vein to side of inferior vena cava	3
5. Side of portal varix to side of inferior vena cava	1
6. Vein graft (superficial femoral) between portal vein and inferior vena cava. (caudate lobe hypertrophy)	1

Lateral portacaval anastomosis for extrahepatic obstruction:—It is in this group comprised for the most part of infants, children, and young adults, that we have used the "make-shift" side-to-side anastomosis. Our results in young

children have been poor for the small size of the vessels available for anastomosis have not remained patent after the construction of a shunt. This is true for the children who have had splenorenal shunts and also for the children having lateral anastomosis of the superior mesenteric vein and the inferior vena cava. We believe that transesophageal ligation is the procedure of choice in these little patients until the age of ten years when their vessels will be larger and permit more satisfactory shunts. There are two such children in this series.

TABLE XI

TYPE SHUNT PERFORMED FOR EXTRAHEPATIC OBSTRUCTION

1. Side of portal varix to side of inferior vena cava	5
2. Side of superior mesenteric vein to side of inferior vena cava	2
3. Omental vein to right renal vein	1

A brighter picture is the young adult who quite often has had splenectomy with or without a splenorenal shunt. We have elected to re-explore these patients and found a fortuitously situated dilated portal collateral in the right free border of the gastrohepatic omentum which we have anastomosed side-to-side to the inferior vena cava. There are three patients in this particular group and all are living without recurrent bleeding two, three, and four years after this "make-shift" type of shunt.

TABLE XII

EARLY OPERATIVE MORTALITY
1-30 DAYS INCLUSIVE

Intrahepatic block		*11*
Coma		8
Wound dehiscence		1
Wound dehiscence with bleeding gastric ulcer		1
Lower nephron nephrosis		1
Extrahepatic block		*0*
Condition of shunt at postmortem		
Patent	3	
Closed	0	

COMMENT

One of us (C.G.J.) has long believed that complete portal diversion was improper because it restores the fetal circulation wherein all of the portal blood is diverted from the liver.

It has been shown in animal experiments that liver regeneration is only half as evident when portal blood is totally diverted, and that there is essentially

no difference between the capacity of portal blood and caval blood in stimulating regeneration. Arterial blood has been found to be unusually effective for favoring regeneration of the injured liver parenchyma[44]. These observations emphasize the importance of adequate perfusion of the liver as the important factor[45]. It is of interest that hepatic coma has been reported in patients without demonstrable liver disease. Under these circumstances there has always been

TABLE XIII

LATE MORTALITY—41 DAYS TO 94 MONTHS

Intrahepatic block (19)		
Hepatic coma	8	9
Bleeding and hepatic coma	1	Directly attributable
Skull fracture	1	to liver disease
Pancreatitis and pylonephritis	1	
Pneumonia	2	
Meningitis	1	
Congestive failure	1	
Coronary artery disease	1	
Miliary tuberculosis	1	
Unknown	2	
Extrahepatic block (0)		
Condition of shunt at postmortem		
Patent 6		
Closed 2		

end-to-side portal diversion as a feature of a radical operation for pancreatic carcinoma[46]. Postmortem examination of those dying in hepatic coma has failed to reveal any evidence of basic liver disease.

There can be little question that the lateral anastomosis is of greater technical simplicity than the Eck fistula or the splenorenal shunt. The Eck fistula

TABLE XIV

NUMBER OF BLEEDING EPISODES POST SHUNT

	1	2	3	Many
Intrahepatic Block	4	1	0	1
Extrahepatic Block	0	1	0	1

demands considerably greater dissection of the portal vein, greater exposure of the tissues in the hilum of the liver, precise ligature of the hepatic stump of the divided portal vein and meticulous positioning of the end-to-side anastomosis to prevent kinking torsion or other obstructive dislocations. The spleno-

renal shunt demands that numerous vascular collaterals be divided and secured, that tributary veins from the pancreas to the splenic vein be individually ligated without compromise of the lumen of the splenic vein and that the implantation of the splenic vein into the renal vein be done without distortion to permit an effective shunt. The splenorenal shunt also demands frequent recourse to venous autografts to supplement the length of a short splenic vein. Too little attention has been paid to the disadvantages of splenectomy. Not only does it increase operating time, but there is the likelihood that it increases thrombosis. It has been demonstrated that visceral excision temporarily reduces portal pressure with resultant decreased flow at the very time when it is needed to maintain patency of the shunt. Associated hypersplenism in portal hypertension is relieved by portacaval shunt as effectively as it is by splenectomy. Recurrent

TABLE XV

SURVIVORS

Duration of Survival	Living and Well		Living, with Bleeding		Living, with Episodes of Coma	
	Intra. bl.	Extra. bl.	Intra. bl.	Extra bl.	Intra. bl.	Extra. bl.
Under 1 year	2	0	0	0	2	0
1-3 years	8	2	0	2	0	0
3-5 years	7	2	0	0	4	0
5-10 years	8	2	0	0	0	0

splenomegaly is an early sign of closure of a portacaval shunt and it seems reasonable that this reservoir function may be a useful safety factor to avoid precipitate recurrence of hemorrhage or to warn the physician of the imminence of recurrent bleeding. For all of these reasons lateral portacaval anastomosis continues to have its adherents (Longmire[31]).

Another possible but still controversial advantage of the lateral anastomosis is the fact that hepatic arterial blood normally flows intermittently into the portal venous system. Longmire suggested that ligation of the portal vein in the hilum of the liver might prevent this reflux and further impair hepatic circulation[31]. Taylor's studies of the response to the Valsalva maneuver also validate this concept[10].

It is impossible to identify a clinical advantage to a given type of anastomosis for the treatment of portal hypertension associated with alcoholic cirrhosis of the liver. Apart from the technical considerations the type shunt performed is of far lesser importance than the interdiction of alcohol and the ingestion of

an adequate diet. Continued chronic alcoholism and progressive liver deterioration insure the early demise of the patient regardless of the surgical management.

Conclusions

1. Transesophageal ligation is the procedure of choice in infants and young children for the control of bleeding esophageal varices. Repeated ligations may

TABLE XVI

Summary of Various Types of Shunts Eck, Splenorenal Lateral Portacaval

	No. of patients	No. of shunts	Operative mortality	Postshunt deaths from hemorrhage	Late deaths other causes	Alive
Blakemore (Eck)						
Intrahepatic	147	No	30(20%)	No	21(14.3%)	96(65%)
Extrahepatic	49	Information	3(6.1%)	Information	2(4.0%)	44(90%)
Totals	196		33(15.8%)		23(11.7%)	140(71.4%)
Linton (Splenoral)						
Intrahepatic	66	69	12(18%)	1(2%)	6(11%)	47(71%)
Extrahepatic	24	25	1(4%)	0	1(5%)	22(92%)
Totals	90	94	13(14%)	1(1.3%)	7(9%)	69(77%)
Welch (Eck)						
Intrahepatic } No				No		
Extrahepatic } Breakdown				Information		
Totals	40	41	6(15%)		11(27.5%)	23(58%)
Patton (Lateral Portacaval)						
Intrahepatic	57	59	11(19.3%)	2(3.5%)	19(33.3%)	27(47.3%)
Extrahepatic	8	11	0	0	0	8(100%)
Totals	65	70	11(16.9%)	2(3.0%)	19(29.2%)	35(53.8%)

be necessary prior to the age of 10 years. It may also be of value when a previously performed shunt has closed.

2. Apart from technical considerations it is impossible to identify a clinical advantage for the lateral portacaval anastomosis. Chronic alcoholism and progressive liver disease cause early demise regardless of the type shunt performed.

The authors express their appreciation to Miss Betty Beech and Miss Lucille Brueser of the Detroit Receiving Hospital for their help in the follow-up of these patients.

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Discussion

Dr. O. H. Wangensteen:—Dr. Patton's idea that it is possible to do a type of glorified Talma-Morison operation, for cases of extrahepatic block giving rise to portal hypertension, is interesting. If Dr. Patton can successfully implant ends of vessels of the size he has described, into the vena cava in cases of cavernoma of the portal vein, he has added something rather important to the therapy of this type of portal hypertension.

It distressed me to note that Dr. Patton observed no suggestion of utility in excision of the acid-peptic-secreting area of the stomach, which procedure, I have been wont to employ for extrahepatic types of portal hypertension. No one will deny that for patients with an intrahepatic block, that a lateral portacaval shunt is the operative procedure of choice. A dozen years ago, I performed total gastrectomy for a boy of 17 with a cavernoma of the portal vein. It required 65 transfusions to put him in shape for the operative procedure. He has remained well these many years, save for a bout with gallstones. In fact, he has graduated from dentistry, practices his profession and has married. About the same time, I did two young boys who had previously undergone splenectomy for what had been regarded as Felty's syndrome. When bleeding recurred, and the presence of a block in the portal vein was noted, there seemed to be nothing else to do other than to excise the entire acid-peptic-secreting area of

the stomach, anastomosing the antrum to the esophagus. These young boys seemed to grow, and developed normally. All three of these patients, of course, take Vitamin B_{12} because they otherwise would have megaloblastic anemia.

There have been failures, of course, with this type of procedure for portal hypertension in the presence of an extrahepatic block. In the instance of a girl who bled following such a procedure, my colleague, Dr. Fletcher A. Miller, subsequently excised the antrum and noted therein a large plexus of mucosal vessels. He excised the antrum, closed the duodenum and anastomosed the esophagus, after excluding it as the source of bleeding, to a loop of jejunum by the Roux-Y method. This patient has remained well. The interposition operation, suggested by my erstwhile colleagues, Drs. H. W. Clatworthy of Columbus (*Surgery* **36**:399, 1954) and K. Alvin Merendino of Seattle (*Ann. Surg.* **141**:201, 1955) is without a doubt a more physiologic attack upon this type of portal block than is total gastrectomy or anastomosis of the antrum to the esophagus. The latter operation, as I just mentioned, leaves the patient with a megaloblastic anemia, necessitating the administration of Vitamin B_{12}. The interposition operation, on the contrary, makes it possible to retain the stomach in a large number of instances.

As most of you know, the observation of Mulligan of St. Louis (*Proc. Surgical Forum* **8**:208, 1957) and of Grossman and his colleagues (1958) would support the idea that the performance of portacaval shunts potentiates the peptic ulcer diathesis. These authors observed recurrent ulcers and hemorrhage after the performance of portacaval shunts, and studies upon dogs with isolated Heidenhain pouches suggests that, secretion from these pouches is enhanced following the performance of portacaval shunts. Nevertheless, no one will doubt the importance of reducing the portal pressure in instance of portal hypertension due to an intrahepatic block.

It perhaps is not out of place for me to point out that, my associates, Drs. Peter A. Salmon and Ward O. Griffen, Jr., have found that intragastric cooling is an agency of merit in massive gastric hemorrhage from bleeding esophageal varices. Some of this benefit is owing undoubtedly to the inhibition of peptic activity, which accompanies gastric cooling. There is, however, also a tremendous reduction in blood flow and when the lower esophagus is cooled, as well as the stomach, one can reasonably understand how the hemorrhage is diminished. Those of you who have not yet tried this expedient will be pleased to observe, I am certain, that it has something to offer.

In the performance of portacaval shunts for intrahepatic block, Blakemore has been at pains to point out that, the preoperative preparation of the cirrhotic patient for the ordeal by restoring lowered plasma proteins by protein feedings —that this expedient is a very important measure of the ultimate success of the shunt. Dr. Blakemore's very success with the method suggests that we would do well to heed his advice.

Surgeons everywhere, I am certain, will watch with a good deal of interest Dr. Patton's interesting and intriguing idea of lowering the portal pressure in instances of extrahepatic block by implanting small veins of the mesentery or of the omentum into the vena cava.

Dr. I. Snapper:—I was deeply impressed by the outstanding paper of Dr. Patton. The hour is late and there is no time for lengthy remarks. Perhaps, however, Dr. Patton will make a short comment about the incidence of ammonia poisoning among his patients.

Dr. T. B. Patton:—Because this ammonia problem is exceedingly important I passed over the fact that in preparing these patients for operation, as Dr. Wangensteen has emphasized, it is necessary, to titrate the amount of protein which is given in the diet against the level of the blood ammonia. I think that if this is not done, we can push these patients into hepatic coma. We find that patients who have a blood ammonia of more than 300 gamma per cent are almost always in coma.

The patients which survived the immediate effects of the operation, did have a blood ammonia greater than 150 gamma per cent and did develop coma. It has been felt that the arginine has a place in the treatment of hepatic coma. There is an article in the current issue of the *American Journal of Medicine* concerning the double-blind study of arginine which would lend doubt to this. The restriction of protein, the sterilization of the gastrointestinal tract, and the rapid flushing of blood from the intestines may be the reason for increasing reports of survival of patients in hepatic coma. We routinely use arginine in treating patients in hepatic coma but we are uncertain as to its place in treatment of this condition at present.

I did want to say it is useless to use a vessel that is less than a centimeter in diameter in the performance of a "make-shift" shunt.

CHAGAS' DISEASE, A POSSIBLE CAUSE OF MEGAESOPHAGUS AND MEGACOLON*

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In 1887 Hirschsprung[1] published his paper describing constipation in the newborn resulting from dilatation and hypertrophy of the colon. Inherent in this description of the disease was his assumption that the dilated portion of the bowel was at fault since no stricture nor stenosis below that segment could be demonstrated. Because a mechanically obstructing lesion is lacking in cases of congenital megacolon the condition was early believed to be the result of some autonomic nervous imbalance. Anticholinergic drugs on the one hand[2], and mecholyl[3] on the other have been used in the medical treatment without consistent results, and surgical treatment by lumbar sympathetic ganglionectomy has been equally disappointing[4].

In 1901 Tittel[5] noted that in a case of megacolon without stenosis in an infant who died at the age of 15 months the ganglion cells of the myenteric plexus at various levels of the large intestine were scanty and showed degenerative changes. He concluded that this abnormality of Auerbach's plexus might have contributed to the development of the megacolon. For many years there was no confirmation of this finding because in each case studied, sections from the grossly abnormal dilated portion of the colon were examined and the undilated sigmoid or rectum ignored. Then in 1920 Dalla Valle[6] reported his observations after examining sections of various portions of the large intestine in two fatal cases of megacolon. In both cases cells of Auerbach's plexus were found in sections of bowel from the dilated segments and above, but were absent in sections from the sigmoid colons, which were of normal size. The evidence that congenital megacolon is caused by absence or destruction of the myenteric plexus of the undilated rectum or sigmoid colon accumulated with contributions by many others, including more recently Tiffin et al[7] and Whitehouse and Kernohan[8]. The condition is now successfully treated surgically by removal of the grossly normal rectum and sigmoid colon, which are deficient in ganglion cells[9,10].

Whitehouse and Kernohan[8] in 1948 not only demonstrated with exactitude the degree to which the number of ganglion cells varied from the normal in various parts of the colon and rectum in congenital megacolon, but also showed that in acquired megacolon and in colons of normal size the ganglion cells were

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normal. It is highly significant therefore that Etzel[11,12], one of the earliest precise investigators, found that in Brazil nonobstructive, acquired megacolon presented the same defects of the myenteric plexus as does congenital megacolon. He found this condition to be frequent and not uncommonly associated with megaesophagus and, because of a high incidence of this association in poor rural areas, became convinced that the two conditions were manifestations of a systemic neural disorder, which he thought was the result of Vitamin B deficiency[13].

It thus appears that there are several types of megacolon—1. congenital nonobstructive megacolon associated with absence of myenteric ganglion cells of the nondilated bowel distal to the megacolon, 2. acquired megacolon, ordinarily due to chronic obstruction not associated with any disorder of the myenteric plexus and 3. acquired megacolon similar in all respects to 1 except with regard to age of onset.

The accumulation of information concerning megaesophagus has not proceeded as rapidly as has elucidation of the nature of megacolon. This may be due to the lower mortality rate in cases of megaesophagus and the inadequacy of our knowledge concerning functioning units of the organ.

Willis in 1672[14] first described a case of megaesophagus and even provided treatment by dilatation, but Hurst (1934)[14] was the first to postulate that the condition was due to destruction of Auerbach's plexus. For years it was thought that the dilatation and abnormal motility of the esophagus proximal to the narrow lower portion were secondary to chronic obstruction resulting from fibrosis, spasm, pressure of the lungs, or pressure from the diaphragm. It is now apparent that the abnormal motility is itself the cause of megaesophagus and for this reason the condition has been termed "aperistalsis"[15]. Within recent times the neurologic origin of megaesophagus has been confirmed by Cross[16] and by Lendrum[17] who demonstrated the marked scarcity or absence of myenteric ganglia in the esophagi removed from cases of cardiospasm.

The analogy of megaesophagus to megacolon is therefore almost complete. What is lacking is adequate information about the nature of the functional segments of the normal esophagus and the fate of the myenteric ganglia in the various parts of the esophageal tube in megaesophagus. At present megaesophagus is treated surgically by either destroying the ability of the circular muscle at the distal end to constrict (by dilatation or by the Heller procedure[18]), or by anastomosing the lower end of the esophagus side-by-side with the cardia of the stomach. The success of these procedures is certainly reminiscent of the results in megacolon when the narrowed rectum and sigmoid colon are removed. It may therefore be that myenteric ganglia are destroyed mostly at the lower end of the esophagus rather than throughout the smooth muscle portion. Keith in 1915[19] reported an autonomic pacemaker for the stomach located at the esophagogastric junction, similar to the sinoauricular node of the heart, which he also discovered. Anesthesia of the lower end of the esophagus abolishes

esophageal peristalsis of the entire esophagus, probably indicating the presence of a "zone of command" of esophageal peristalsis at the esophagogastric junction[15].

In Brazil both megacolon and megaesophagus are common. In fact, many patients have both conditions simultaneously. It will be recalled that Etzel demonstrated that the acquired megacolon of Brazil, like megaesophagus and congenital megacolon, was characterized by a deficiency of myenteric ganglia in the narrowed portion of the alimentary canal distal to the dilatation. The geographic distribution of megacolon in Brazil by which Etzel sought to prove the role of avitaminosis in the disease serves equally as well to suggest Chagas' disease as a possible cause[11,12,13].

Chagas' disease is infection with the American trypanosome, *Trypanosoma cruzi*[20]. It is transmitted by blood-sucking bugs of the family, *Triatomidae*. Two forms of the parasite exist in the mammalian (including human) host—the motile flagellate form, found in the blood, and the rounded leishmania form, which multiplies intracellularly in various tissues. The acute phase of the infection, which is seen uncommonly, produces swelling at the site of inoculation, fever, debilitation, and myocarditis. It is quite likely that the acute phase often is mild, subclinical or mistaken for other febrile illnesses. The late chronic infection is well known to be associated with cardiac disease. The heart is greatly enlarged, with remarkable thickening of the walls of the ventricles except at the apex where there is thinning and fibrosis.

The basic defect in heart disease due to chronic American trypanosomiasis appears to be in the conducting system—right bundle branch block being particularly characteristic. Sinoauricular block has also been observed, apparently resulting from damage to the ganglion cells in the node of Keith[21].

Diagnosis can be made in the acute phase by demonstration of the trypanosomes in blood films, by culturing the organism on proper media, by animal inoculation and by xenodiagnosis (infecting the vector *via* a blood meal). The organisms may be found in tissues at any stage but become scarce late in the infection. Late infection is therefore best diagnosed by the complement-fixation test.

Stimulated by the suggestive evidence that megacolon and megaesophagus occur very commonly in parts of Brazil where Chagas' disease is common, certain scientists have sought additional data to connect the diseases. De Freitas showed that in 95 per cent of cases of megaesophagus and megacolon in Brazil the complement-fixation test for American trypanosomiasis was positive[22], whereas the test is known to be positive in random samples in only about 20 per cent of the population of the district in which he worked. Köberle[22,23] studied the myenteric ganglia in acute and chronic Chagas' disease both in experimental animals and in man and found that the disease is characterized

by periodic invasion by the parasites of the smooth muscles. After five days of intracellular development the parasites destroy the host's muscle cells and invade the interstitial tissue. The motile forms immediately enter the circulating blood but many of the leishmania die. Köberle believes that he has obtained histopathological evidence that a toxin is liberated from the dying organisms which specifically destroys the ganglion cells of the myenteric plexus. Presumably the same mechanisms may destroy the sinoauricular node[21].

The importance of this provocative information to the American gastroenterologist lies in the fact that human Chagas' disease is now known to occur in this country. For many years wild animals and triatomid bugs infected with *T. cruzi* have been found in the southwestern United States from California through Texas. In 1956 the parasite was found in naturally infected raccoons near Washington, D. C.[24] and in 1957 organisms resembling *T. cruzi* were isolated from wild animals collected in Georgia[25]. Of more significance was the discovery of two human cases of Chagas' disease in Texas[26,27].

While it is not generally accepted by Brazilian workers that megaformations represent an essential feature of Chagas' disease, still the evidence is highly suggestive that this is so. The parasitic infection may thus be partly responsible for the megaesophagus and acquired megacolon seen in this country. Unfortunately, demonstration of American trypanosomiasis to be the cause of megaesophagus or megacolon would benefit the patient little at present since there is no effective treatment for the infection. On the other hand recognition of endemic Chagas' disease would be of considerable value since prevention can be accomplished by eradication of the insect vectors or avoiding exposure to their bites.

Summary

Both megaesophagus (cardiospasm) and megacolon have been shown to be due to deficiencies in the myenteric plexus. In Brazil evidence has been adduced to relate these diseases to Chagas' disease which is now known to occur also in the United States. It is thought that a toxin elaborated by the dying leishmanias specifically damages the myenteric ganglion cells. Chagas' disease must now be considered as a possible cause of megaesophagus and megacolon in this country.

Addendum

At the very time that this paper was being presented, my colleague at Tulane Medical School, Dr. Antonio D'Alessandro Bacigalupo demonstrated *T. cruzi* in the blood of animals captured in Louisiana near New Orleans. He has isolated this organism from three out of six raccoons and two out of three opossums and has demonstrated its pathogenicity in mice of various ages.

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Discussion

Dr. I. Snapper:—This paper is highly interesting to me because, as I have stated several times at previous sessions of this course, I have always felt that a

preceding polyneuritis may play an important role in the etiology of achalasia of the esophagus. I have observed repeatedly that persons who had suffered from postdiphtheritic neuritis later developed achalasia of the esophagus. Dr. Jung's very interesting paper about the connection between the polyneuritis of Chagas' disease, megacolon, and megaesophagus, seems to indicate that there is some merit in this old concept.

Dr. Rodney C. Jung:—A question was handed to me: Do complement fixation studies show any megacolon to be due to Chagas' disease in this country?

Well, the complement fixation studies in general in this country have been negative, and we are working on this problem at present. Complement-fixation using the same antigen as used in some North American surveys has been tried in several instances in places in South America where the disease is known to occur, also with negative results, indicating that some of the complement-fixation surveys done here might have been faulty.

We are now in the process of setting up the test here in the hope that we will be able to provide an answer to this problem, so it certainly has not been proved, but the interesting thing about the history of Chagas' disease is that it has always been overlooked in all parts of the world where it is now known to occur. It has not been recognized until deliberate efforts have been made to detect it.

Two acute cases of Chagas' disease have occurred in Texas. In those places where Chagas' disease is known to occur, the acute case is found with only a fraction of the frequency that the chronic case is seen.

I am sure that the reason Chagas' disease will not be found as commonly in this country as in other places where the organism occurs is due to the higher standard of living here which reduces opportunity for exposure, but I think that its presence is a possibility which should be pursued further.

THERAPY OF STRONGYLOIDIASIS WITH DITHIAZANINE*

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According to Stoll's estimate there are 35 million persons infected with *Strongyloides stercoralis* in the world. The estimated number of infections in this country is 400,000; most of these are in the southern states[1]. Because of the relative frequency of strongyloidiasis and since the parasite can produce pathology and clinical disease in humans, an effective form of therapy has been sought for decades.

The life cycle of *S. stercoralis* differs in some respects from other common nematodes parasitic in man. Human infection begins with local penetration of the skin, usually of the feet. The larvae migrate to a small vessel and are carried to the lungs. Pulmonary infiltration can give rise to bronchopneumonia or to a scattered patchy type infiltration (Loeffler's pneumonia). Such pulmonary findings are not frequently manifested clinically. In either instance the maturing larvae continue their course, this time along the respiratory tree to the epiglottis. With deglutition the parasite is carried to the upper small intestine where the adult worms may enter the mucosa and begin to oviposit. Ordinarily the rhabditiform larvae are passed in the stool. Enroute down the intestine, however, sometimes they can transform into the filariform stage. This latter form is capable of penetrating the colonic or perianal mucosa and giving rise to internal or external autoinfection, respectively. Thus larvae can again enter the circulation, traverse the pulmonary tree and ultimately reach the small intestine. In this manner the patient's worm burden can increase or be replenished even though he may never again come into contact with infested soil. It can easily be seen that once acquired such an infection can continue for many years and, protected by favorable internal environmental conditions, can persist in any climate.

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The drug employed in this study, dithiazanine (Delvex, Telmid), was provided by Eli Lilly and Company.

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Jones[2], in a review of 100 cases, described precisely the symptoms and signs associated with human strongyloidiasis. He found that pain in the epigastrium, nausea, vomiting, anorexia, diarrhea and fatigue were common complaints. Urticaria also is a relatively common finding in this disease although uncommon in the other roundworm infections. In severe clinical infections excessive weight loss and protracted diarrhea may occur and invalidism ensue. Fatalities have been reported but are exceedingly rare.

TABLE I

Admission Diagnosis	Number of Cases
Strongyloidiasis	5
Peptic ulcer	4
Bronchogenic carcinoma	2
Emphysema	2
Bronchiectasis	2
Cirrhosis	1
Cholelithiasis	1
Irritable colon	1
Hemorrhoids	1
Inguinal hernia	1
Bronchopneumonia	1
Tuberculosis	1
Arteriosclerosis	1
Cerebral thrombosis	1
Aseptic meningitis	1
Herniated nucleus pulposus	1
Syringomyelia	1
Melanoma	1
Chorioretinitis	1
Cataracts	1
Basal cell carcinoma	1
Depressive reaction	1
Total	32

Apart from finding the larvae on examination of fecal specimens or duodenal aspirate, two other laboratory findings are of interest and suggest the infection. The first is a peripheral eosinophilia. This occurs quite commonly and the degree of eosinophilia can be startling. The second finding is that of a duodenitis associated with the mucosal location of the adults and their progeny. This may be detected radiographically during barium studies of the upper gastrointestinal tract. A spastic and coarsened mucosa is found in the duodenum and the organ is photographed only with difficulty. In Louisiana where strongy-

loidiasis is common, such a radiographic finding warrants fecal examination and, if necessary, duodenal drainage.

Through the years many drugs have been used in an attempt to cure strongyloidiasis. Among the earlier preparations employed were thymol, carbon tetrachloride, santonin, dihydranol and oil of chenopodium. Gentian violet has received wide usage for over 20 years. More recent drugs tried include miracil D, phenergan, piperazine, diethylcarbamazine and mantomide. None of these drugs were consistently effective when subjected to accepted criteria for cure, namely, permanent disappearance of larvae from the stool and duodenal aspirate.

Recently a new oral preparation, dithiazanine (3,3′ diethylthiadicarbocyanine iodide, Lilly), was developed which was shown to be highly effective against various helminth infections in laboratory animals by McCowen et al[3]. Simultaneously, Frye et al[4] demonstrated the drug to be effective against human trichuriasis. The scope of investigation was then enlarged by Swartzwelder et al[5,6] to embrace human trichuriasis, enterobiasis, strongyloidiasis, ascariasis, and hookworm infections and murine strongyloidiasis. The results clearly indicated that this drug was truly a broad spectrum anthelmintic with particular efficacy against trichuriasis, strongyloidiasis, enterobiasis and ascariasis.

To be presented in this paper are the results of treatment of 32 cases of strongyloidiasis. The method of investigation will be outlined, selected clinical cases will be summarized, and results of autopsy in two cases will be reviewed.

Methods:—Since this study was made in a Veterans Administration Hospital, all of the patients treated were males. Twenty-six of the patients were white and six were negro. In addition to strongyloidiasis, these patients exhibited a wide variety of other diseases. This can be appreciated by referring to Table I which lists the admission diagnoses.

Before treatment with dithiazanine was initiated, extensive laboratory tests were done. Several stool specimens and at least one duodenal drainage were performed. Other laboratory studies included hemogram, urinalysis, blood urea nitrogen, and liver profile tests (bilirubin, cholesterol, alkaline phosphatase, zinc, lipid and thymol turbidities, prothrombin time, cephalin flocculation and bromsulfalein excretion). A total eosinophil count was done in several instances. During and after treatment an attempt was made to repeat the above tests weekly. Multiple stool specimens and duodenal aspirations were done, the number of the latter depending upon the patients' willingness to accept the procedure.

Direct fecal smear and formalin-ether centrifugal concentration technics were employed on all stools. Formalin-preserved fecal specimens were submitted by some patients after their discharge from the hospital as part of a post-treatment examination routine.

The duodenal drainages were accomplished in the usual manner by having the patient swallow a metal tipped tube (Rehfuss). Then while lying on the right side the tube was slowly advanced into the duodenum. When indicated, fluoroscopy was employed to place the tube into the duodenum. In two of the patients a jejunal drainage was necessary due to previous gastrojejunostomy. Each specimen of drainage fluid was examined by three persons before being considered negative for parasites.

Additional technics were occasionally employed. These included stool examination by the zinc sulfate centrifugal flotation method, culture of fecal samples in bone charcoal, and digestion of duodenal aspirate with chlorox (sodium hypochlorite) solution with examination of the resultant sediment for larvae.

In three instances associated medical illnesses resulted in death of the patient. In two of these cases an autopsy was performed. At postmortem examination numerous wet smears of material from the mucosa of representative areas of the duodenum were examined for larvae. Then the mucosa of the entire duodenum was removed by scraping, mixed with water, and allowed to autolyze for one hour at 37°C. The sediment was examined under a dissecting microscope for parasites.

Therapy:—Dithiazanine was administered in tablet form in 29 cases; a suspension of the drug was used in 3 cases. The tablets contain 50, 100, and 200 mg. of the drug enveloped by a special protective enteric coating designed to release the drug after passage through the stomach. The flavored suspension contained 20 mg. of the drug per milliliter. The drug is not readily absorbed and is excreted with the stool to which it imparts a green to blue color.

Initially a dosage schedule of 200 mg. of the drug was given three times daily for five days. Each dose was given two hours after meals. Later the treatment period was extended to 21 days. The lengthened course was necessary because it became obvious that a five-day course of therapy was inadequate to effect a cure. Also it was realized that such a short course of therapy would have no effect on larvae migrating extraintestinally as a result of internal or external autoinfection. Thus reinfection of the upper small intestine might occur after the five-day course was terminated. Once the 21-day course was demonstrated to be adequate the dosage was reduced from 600 to 300 mg. per day. Evaluation of the efficacy of the latter dosage schedule is continuing. One patient received treatment beyond 21 days. This case, to be summarized later, was treated for 29 days and expired of bronchogenic carcinoma on the 30th day.

Results:—Diagnostic forms of *S. stercoralis* were not demonstrable after therapy in stools and duodenal drainage aspirates in 29 of the 32 treated patients. The cure rate in this series was 90 per cent. Table II lists the form of therapy given, the results of pre- and posttreatment examinations of the feces

TABLE II

Case	Pretreatment		Days of treatment	Dosage in grams	Posttreatment		Duration of follow-up	Reactions	Treatment failure
	Stool	Drainage			Stool	Drainage			
1	Pos.	Neg.	5	3.0	21 Neg.	1 Pos.	1 Mo.		Yes
1a	Neg.	Pos.	21	12.6	17 Neg.	4 Neg.	10 Mos.		No*
2	Pos.	Neg.	21	12.6	8 Neg.	—	1 Mo.		No
3	Pos.	Pos.	5	3.0	11 Neg.	4 Neg.	6 Mos.		No
4	Pos.	Pos.	21	12.6	18 Neg.	5 Neg.	9 Mos.	Diarrhea	No
5	Pos.	Pos.	21	12.6	11 Neg.	5 Neg.	12 Mos.		No
6	Pos.	Pos.	6	3.6	13 Neg. 2 Pos.	1 Pos.	2 Mos.		Yes‡
7	Pos.	Pos.	21	12.6	15 Neg.	5 Neg.	6 Mos.		No
8	Pos.	Pos.	5	3.0	5 Neg. 1 Pos.	2 Pos.	2 Mos.		Yes
8a	Pos.	Pos.	21	12.6	—	1 Pos.	1 Mo.		Yes
9	Pos.	Pos.	5	3.0	15 Neg.	2 Neg.	10 Mos.		No
10	Pos.	Pos.	5**	3.0	2 Pos.	1 Neg.	1 Wk.		Yes
10a	Pos.	Neg.	5**	3.0	5 Neg. 1 Pos.	1 Neg.	14 Mos.		Yes
10b	Pos.	Pos.	21	12.6	16 Neg.	3 Neg.	3 Mos.		No
11	Pos.	Pos.	8**	4.8	33 Neg.	7 Neg.	6 Mos.	Diarrhea	No
12	Pos.	Pos.	21	12.6	7 Neg.	2 Neg.	10 Mos.		No
13	Pos.	Pos.	21	12.6	32 Neg.	5 Neg.	10 Mos.		No
14	Pos.	Pos.	5	3.0	13 Neg.	3 Neg.	3 Mos.		No
15	Pos.	Pos.	21	12.6	17 Neg.	4 Neg.	9 Mos.		No
16	Pos.	Pos.	21	12.6	6 Neg.	3 Neg.	2 Mos.		No
17	Pos.	Pos.	21	12.6	20 Neg.	5 Neg.	11 Mos.		No
18	Pos.	Pos.	21	12.6	19 Neg.	2 Neg.	8 Mos.		No
19	Pos.	Pos.	21	12.6	17 Neg.	5 Neg.	11 Mos.	Vomited	No
20	Pos.	Pos.	21	12.6	27 Neg.	4 Neg.	3 Mos.		No
21	Pos.	Pos.	21	12.6	30 Neg.	3 Neg.	10 Mos.		No
22	Pos.	Pos.	21	12.6	9 Neg.	3 Neg.	2 Mos.		No*
23	Pos.	Pos.	21	12.6	13 Neg.	2 Neg.	2 Wks.		No
24	Pos.	Pos.	21	6.3	18 Neg.	2 Neg.	2 Mos.		No
25	Pos.	Pos.+	21	6.3	16 Neg.	3 Pos.	1 Mo.		Yes
26	Pos.	Pos.	21	6.3	12 Neg.	4 Neg.	5 Mos.		No
27	Pos.	—	29	8.7	10 Neg.	—	—		No*
28	Pos.	Pos.+	21**	12.6	18 Neg.	5 Neg.	4 Mos.	Vomited	No
29	Pos.	Pos.	21	6.3	9 Neg.	3 Neg.	2 Mos.		No
30	Pos.	Pos.	21	12.6	16 Neg.	4 Neg.	4 Mos.		No
31	Pos.	Pos.	21	6.3	6 Neg.	3 Neg.	1 Mo.		No
32	Pos.	Pos.	21	12.6	9 Neg.	4 Neg.	1 Mo.		No

*Patient expired from causes unrelated to therapy.
**Received dithiazanine in suspension form.
‡Treatment discontinued.
+Jejunal drainages performed.

and duodenal drainage aspirate and the length of the follow-up observation period.

As noted, two of the patients required retreatment before a cure was obtained. One patient (Case 10) was retreated on two occasions for 5 and 21 days. The second patient (Case 1) required only one additional period of retreatment for 21 days.

Treatment failure occurred in three patients. The first (Case 6) received the medication for only 6 days. Treatment was then discontinued because of the development of a depressive psychosis which was unrelated to therapy. The second patient (Case 8) was treated for 5, then 21 days at which time rhabditiform larvae of *S. stercoralis* could still be found in the duodenal drainage aspirate. The third patient (Case 25) had had previous gastric surgery with gastrojejunostomy; larvae were still demonstrable after 21 days of treatment. It is possible that the altered anatomic relations coincident to the gastrojejunostomy resulted in diverting the medication away from the afferent loop where most of the parasites are known to reside.

The drug was well tolerated. Two patients had mild and evanescent diarrhea without cramping during treatment. One patient vomited twice during a 21-day course of medication. Intolerance was noted in Case 28 who had a gastrojejunostomy. He exhibited nausea, occasional vomiting and epigastric pain throughout the 21-day regimen. As he received the liquid suspension, it is postulated that a gastritis was induced or aggravated. In none of the cases did any alteration occur in the determination of the hemogram, urinalysis, blood urea nitrogen, or liver profile tests which might be attributed to drug toxicity.

A peripheral eosinophilia was noted in 16 of the 32 cases. The highest value was 55 per cent. In most of these cases eosinophilia provided the clue which, in the absence of other clinical data, led to stool and drainage examination. During the latter phase of the study total eosinophil counts were performed before and after treatment. A progressive decrease in the count was observed in every case.

During and following treatment, clinical improvement was seen in a few cases. Since, however, other patients in this series had no symptoms referable to the abdomen or gastrointestinal tract, no over all assessment of improvement could be made.

The following case summaries have been selected to illustrate specific considerations. The first two cases represent fairly typical cases of human strongyloidiasis with response to therapy.

Case 1:—The patient, a 41-year old white male was admitted in January, 1958 for evaluation of abdominal and pulmonary complaints. These began in 1941 while serving in the Armed Forces. At that time he noted the onset of

cramping abdominal discomfort, anorexia, diarrhea and bloating. After the symptoms had continued for several years, he was hospitalized and told he had a duodenal ulcer and strongyloidiasis. He was placed on an ulcer regimen and given gentian violet. The latter treatment failed to cure the parasitic infection. The pulmonary complaints consisted of wheezing and productive cough which occurred during the winter months and were diagnosed as asthma. Bronchodilator drugs gave only partial relief. He described recurrent attacks of pneumonitis for which antibiotics were administered.

Fig. 1—Case 1. Duodenitis associated with strongyloidiasis. The entire duodenum was found to be spastic and exhibited coarsened mucosa.

Physical examination:—The patient appeared thin and slightly undernourished. Musical rales and coarse rhonchi were heard bilaterally on auscultation of the lungs. The expiratory phase of respiration was prolonged. The second pulmonic sound was accentuated. The epigastrium and right upper quadrant were tender to palpation. No organs or masses were palpated. Although not present at the time of this examination, the patient described recurrent pruritic perianal urticarial lesions.

Laboratory data:—The total leucocyte count was 15,200 per cu. ml. of which 55 per cent were eosinophils. The total eosinophil count was 6,700 per cu. ml.

A 12-hour sputum collection was examined. Filariform larvae of *S. stercoralis* were found. Rhabditiform larvae of *S. stercoralis* were numerous in the feces and duodenal drainage aspirate. An upper barium meal was reported as showing duodenal cap deformity, coarsening, spasticity and irregularity of the entire duodenum compatible with a duodenitis (Fig. 1).

Course in hospital:—On 16 January 1958 the patient was started on dithiazanine 200 mg. three times daily, each dose being administered two hours after meals. Therapy was continued for 21 days. No untoward reaction was encountered. Four days after therapy was instituted larvae disappeared from the feces. Twelve other fecal specimens were negative. Three duodenal drainags were done during and after treatmnt and no larvae were detected. The total eosinophil count dropped precipitously (Fig. 2). The patient noticed gradual disappearance of the anorexia, abdominal pain and diarrhea. The asthmatic symptoms, however, continued unabated.

Case 2:—This patient was a 34-year old x-ray technician. He too was admitted specifically for treatment of strongyloidiasis. The diagnosis had been established years before when he noted the onset of mid-abdominal cramping pain aggravated by meals. From time to time he was incapacitated by nausea, anorexia and abdominal pain. Many drugs were tried in an attempt to eradicate the infection without avail. Many rhabditiform larvae of *S. stercoralis* were found in fecal sample and duodenal drainage aspirate. Dithiazanine, 200 mg. t.i.d. was given for 21 days. No side reactions were experienced during therapy. Daily stool specimens were examined and by the eighth day no parasites could be found. Nineteen additional stool specimens were similarly negative for parasites. Four duodenal drainages were negative. The abdominal symptoms subsided completely and the patient gained 15 pounds.

As mentioned earlier three deaths, due to associated medical illnesses and entirely unrelated to strongyloidiasis or to therapy, occurred during the period of this study. In two cases autopsy study was permitted. A short summary of the findings are presented below.

Case 3:—This patient was admitted to the hospital for treatment of far advanced bronchogenic carcinoma. In addition to the neoplasm a partial pneumothorax was present. Larvae of *S. stercoralis* were noted on routine stool examination. Because of his combined pulmonary pathology a duodenal drainage was not attempted. He was given intravenous nitrogen mustard as palliative treatment of the neoplasm. Dithiazanine, 100 mg. t.i.d., was given as treatment for the strongyloidiasis. The patient tolerated this medication well and had no reaction. His condition was deteriorating rapidly because of carcinoma and it was decided to continue the drug beyond 21 days. He expired on the 30th day of therapy. At autopsy, extensive metastases of the bronchogenic carcinoma were noted to involve the lymph nodes and liver. The duodenum and upper

jejunum were examined directly for evidence of parasites. After none were found the mucosa of the duodenum was scraped, mixed with water and allowed to autolyze for one hour at 37°C. The material was then examined under a dissecting microscope. No larvae, adults or remnants of parasites were found. No staining of any of the abdominal organs was noted. Although the contents and adherent mucus in the intestine were colored by the dye, the mucosa was not stained. Histologic examination of the intestine and other organs showed no abnormality other than that related to the neoplasm and pneumothorax.

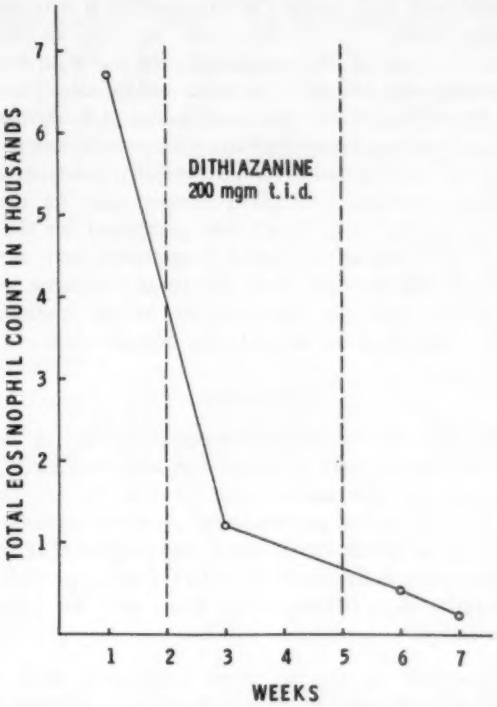

Fig. 2—Case 1. Response of total eosinophil count following treatment of strongyloidiasis with dithiazanine.

Case 4:—This patient was a 61-year old white male who was suffering from syringomyelia. Earlier examination had disclosed strongyloidiasis. Accordingly, when the medication became available for investigational use treatment was begun. A five-day treatment was given initially but larvae were still present at the conclusion of therapy. A 21-day course using dithiazanine, 600 mg. daily was begun. On this occasion the larvae disappeared from the feces and duodenal drainage. Seventeen stool examinations and five duodenal drainages were

negative over a 10-month period. Gradual deterioration of the patient's condition occurred due to the syringomyelia and he expired in February, 1958. Autopsy study was permitted. The duodenum and upper jejunum was examined in the manner described in Case 3 and no parasites could be detected.

The last case to be described demonstrates how the diagnosis of strongyloidiasis may enter into the differential diagnosis.

Case 5:—This 61-year old white male was admitted with the complaints of weight loss, chest pain and cough. On examination it was apparent that pulmonary pathology existed on the right side. An x-ray of the chest disclosed pleural effusion and parenchymal involvement of the right lung. Rhabditiform larvae of *S. stercoralis* were found in the stool and duodenal drainage. A 12-hour sputum sample was obtained and filariform larvae of *S. stercoralis* were found. A diagnosis of pulmonary strongyloidiasis was entertained. A few days later, however, a scalene node biopsy revealed extensive infiltration with anaplastic carcinoma. Nitrogen mustard was given intravenously for the carcinoma and dithiazanine 600 mg. daily (21 days) was prescribed for the strongyloidiasis. After three days of treatment the larvae disappeared from the feces. Fourteen consecutive stool specimens and three duodenal drainages were negative for parasites. The larvae were not demonstrable in the sputum. He expired in September, 1957. Permission for autopsy was not obtained.

Summary

Dithiazanine (3,3′ diethylthiadicarbocyanine iodide) is an effective therapeutic agent for strongyloidiasis. The infection was elminated in 90 per cent of the patients treated with this anthelmintic. Criteria for cure included examination of a series of stools and of posttreatment duodenal drainage fluid from each patient. The dosage of dithiazanine which was employed in most of the cases was 200 mg. three times daily for 21 days. In the latter part of the investigation the dosage was reduced to 100 mg. three times daily for 21 days without loss of therapeutic efficacy.

The side reactions to therapy were infrequent, mild and evanescent. Autopsy study was performed on two patients who expired from causes unrelated to therapy. Thorough examination of the upper small intestine revealed no parasites, providing additional and conclusive evidence of eradication of the infection.

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Discussion

Dr. I. Snapper:—The treatment of strongyloidiasis until now has not been successful. Gentian violet has been recommended for more than 30 years but I have never seen any favorable effect of this treatment.

In certain parts of the world—for instance, in Indochina—strongyloidiasis is a very common cause of severe diarrhea. This parasite also causes tropical eosinophilia. Under the circumstances we must be happy that this new drug is active in the dangerous forms of this widespread disease.

CERTAIN RELATIONSHIPS OF THE IRRITABLE COLON*

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INTRODUCTION

During the past 20 years, clinicians have tried to crystallize a modern, dynamic concept of a syndrome that is called the irritable colon[5]. It is only natural that there be an advance of knowledge in this direction because of the parallel growth of investigation into the two fields that supply the tools for understanding of the colon. One of these is the widening of insight into the autonomic nervous system and the other is the growth of the field of psychiatry, and the awareness of the relationship of emotion, the autonomic nervous system and end organs such as the large intestine. Instead, therefore, of accepting the large intestine as an insignificant structure with minimal physiological function i.e., a tube that absorbs some water and serves mainly as a mechanical channel, the modern physician has been trying to prove with his new tools, what has seemed evident to the observers of the past. The modern physician has been trying to show that functions of the colon constantly reflect man's emotions. Irritability of the colon is a common cause of symptoms that disturb patients, a consistent part of emotional disturbance.

The syndrome of the irritable colon is so new, so difficult to demonstrate by tests or in pathological change, that it often escapes the attention of our medical students and many of our physicians who are trained in specialties. The teaching clinics, overwhelmed with advanced organic diseases, rarely mention it in differential diagnosis. Too often, anxiety and psychiatric diseases are still considered disease of the brain, without effect on the body. There has not been enough awareness that emotional illness or emotional upset always upsets the autonomic, as well as the voluntary nervous system, causing symptoms and signs with secondary organic changes. On the other hand, our understanding of the disturbances of the autonomic nervous system and resulting symptoms, is still so incomplete and recent that there are still numerous aspects that have not been completely made clear by research and scientific technics. Certainly, there are many new syndromes, secondary to emotional disturbances, emerging as we chart further dysfunction of the autonomic nervous system.

At all times, in medical clinics and teaching situations, it seems to me that every symptom presented by a patient should be explained physiologically as well as possible. It is not enough to dismiss numerous disturbances of a labile vascular system or gastrointestinal dysfunction, by terming them an anxiety

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reaction without working out the involved physiological changes. When the clinician does follow this ritual of analyzing each symptom, he will find numerous areas where the explanation for symptoms, which are common and daily in occurrence, is not satisfactory.

I should like to point out some of the areas of dysfunction of the colon secondary to autonomic imbalance and emotional upset, which are not clearly presented in our medical texts or literature. I should also like to review some of the more subtle elements of colonic dysfunction and show the interrelationship with cardiovascular disturbances.

Definition of Irritable Colon

The irritable colon, by definition, is a nonorganic functional disturbance of the colon. There may be increased spasm, hypermotility or increased secretion, all due to autonomic imbalance. Bowel symptoms that result from irritability of the colon will depend on which one of the three elements predominate. The autonomic imbalance is attributed to emotional upset. It should be clearly stated at this time that the irritability of the colon, however dramatic may be its symptoms, is part of a generalized emotional reaction and the physician should look carefully for the other symptoms which are part of this reaction. These include headaches, neckaches, sighing respiration, "lump in the throat", and numbness and tingling of the hands, dizziness, spots before the eyes, tremor, sweating, fatigue, "going to bed tired and waking exhausted", palpitation, aching pain under the left breast with soreness to touch, blackout spells. These symptoms will be present in varying degree and are due to overactivity of voluntary and involuntary nervous systems. When recognized, then successful management of the patient takes them into account. To be discussed later is the fact that spasm of the colon with distention by a peristaltic wave may cause vagovagal reflex with aggravation of many of these symptoms.

Irritability of the colon can manifest itself as involving small, shifting areas of the large intestine, with usually lesser involvement of the entire large intestine and also small intestine. Since the basic difficulty is increased vagus nerve discharge, most areas supplied by the vagus show results of this hyperactivity. Such concomitant symptoms and signs as a slow pulse, cold hands and feet, clammy skin, marked weakness, reveal hypervagotonia. Moderate and mild cases show a shifting of colonic symptoms from one area to another. These patients also have heartburn, indicating involvement of the upper gastrointestinal tract—a part of the same mechanism. Not infrequently, increased sympathetic discharge contributes its effects such as palpitation, change in blood sugar, etc.

There are three distinct syndromes, depending upon which anatomic section of the colon is primarily involved.

The best known of these involves disorder of the sigmoid and descending colon. Common in this area, which is the most frequently disturbed, are the

symptoms of pain of varying severity, constipation, often alternating with diarrhea, and passage of mucus. The pains are bearing-down, sticking and aching. They can occur anywhere in the lower part of the abdomen, but are most common in the midline and to the left. Severe cases have pain over the lower sacral area radiating down toward the anus. Diverticulosis of the colon is found in these patients with a long history of symptoms of an irritable colon, involving the descending and sigmoid colon. Diverticulosis is an organic change in the bowel secondary to the mechanical strain placed upon it by long years of spasm and dysfunction of motility. Diverticulosis most commonly involves the descending and sigmoid colon. Isolated diverticuli can occur in other sections of the colon due to the same play of forces. Because of this etiological background for diverticulosis, therapy should be based on the awareness of the part played by the irritable colon; yet our texts and literature give little explanation or emphasis for this chain of events. When the diverticulosis becomes complicated with diverticulitis, proper management should heavily emphasize the etiological role of the irritable colon. Most texts dismiss diverticulosis as an incidental finding in a certain percentage of people over 40 with little regard for the dynamics behind its origin. Spastic constipation may be mentioned, but there is no comprehensive presentation of the relationship of this local colonic disturbance to the over all emotional background. Perhaps, with more attention given to these dynamics, we can decrease the incidence of these outpouchings and improve our therapy. Today, more stress and understanding should also be placed upon the fact that it is similar irritability of the colon with spasm that contributes to hemorrhoids, and we shall do more to prevent their formation. Both of these conditions—diverticulosis and hemorrhoids—I consider organic changes secondary to long-standing physiological dysfunction of the lower colon.

The second syndrome of the colon involves the cecum and ascending colon to the region of the hepatic flexure. This syndrome has not been given any attention in recent years and, in fact, has not been separated as an entity. Back in 1909, Holzknecht[3] commented on the intestinal mass movement which consisted of sudden relaxation of a physiological sphincter near the hepatic end of the transverse colon with simultaneous contraction of the musculature of the cecum and ascending colon. This phenomenon is similar to the well known gastrocolic reflex. It is recognized that following eating of the breakfast meal, there is a reflex mass movement which prepares the colon for evacuation. The presence of a physiological sphincter in the hepatic end of the transverse colon is not accepted today. It seems to me that some instances of iritable colon may involve dysfunction of such a mechanism of the cecum and ascending colon. Clinically, these patients complain of pain in the right lower quadrant and right upper quadrant, also bloating, and often notice the bulging of the distended cecum. Significantly, this syndrome is often associated with ovarian dysfunction in young women. Many young women, who have been operated on for a gynecological disease of the right ovary, actually have an emotional upset with

dysfunction of the cecum and ascending colon. Whether the ovarian dysfunction is due to secondary changes in the ovary lying next to a distended cecum, or whether it is due to generalized anxiety reaction, I do not know. Clarification of this problem may help us stop needless surgery involving the right ovary. With further development of this syndrome, there may also result avoidance of excessive surgery of the appendix and gallbladder. Many patients with such "typhlitis"—like dysfunction, have been subjected to removal of these two organs when the symptoms were due to the colon. Since x-rays of the irritable colon are usually negative, the diagnosis must be made from history, physical examination and negative laboratory information. The finding of gallstones seems to be enough justification at this time for surgery even though the symptoms may come from some other disorder. Gallbladder disease may contribute to colonic dysfunction, but too often there is no relationship as is well proven by hindsight in many who have had the gallbladder removed.

The third syndrome has received considerable attention lately and has been called the "splenic flexure syndrome". This group has aroused interest because its symptoms can cause much confusion with those due to coronary artery disease. The cause of symptoms in this syndrome has been attributed[4] to the trapping of gas in the splenic flexure and distention of the splenic flexure with severe pain, in the left upper quadrant, the precordial area, the left shoulder, the left side of the neck, the left arm, the jaw, the scapular area and the ulnar side of the left hand[4]. The pain or discomfort is bearing-down, aching, pressing and bloating. Other associated symptoms are palpitation, clammy skin, pallor, dizziness, fainting, marked weakness, blurring of vision. Here again, these are part of the over all primary autonomic upset or are due to the distention of the splenic flexure. It seems to me that the best explanation[4] is that these people have an area of spasm in the descending colon and that this spasm causes the accumulation of gas in the splenic flexure. Waves of peristalsis, trying to force air around this redundant, acutely-angled flexure, cause distention of the bowel with pain and secondary vagovagal reflex, causing weakness, clammy skin, slow pulse, etc. The combination of these symptoms causes marked apprehension, which sets up a vicious cycle, increasing the emotional upset which increases the spasm, aggravating all the symptoms. It may take an injection of Demerol to relieve these attacks. The patient notices relief with the passing of flatus, enema or bowel movement. Explanation of the pain radiation in these patients is not clear. Many physicians would hesitate, when examining a 50-year old patient with precordial pain that goes to the left shoulder and down the left arm, to diagnose this condition as noncoronary. Why does distention of the splenic flexure cause pain in the left shoulder and down the left arm? Is this pain due to the force exerted by the distended loop upon the left leaf of the diaphragm? It has been observed that patients with anxiety reaction and heart consciousness, neurocirculatory asthenia (NCA), have tonic contraction of the diaphragm[6]. Patients with splenic flexure syndrome may fall into this neuro-

circulatory asthenia group, a distinction being that the NCA's have increased sympathetic tone, whereas the splenic flexure syndromes have more vagal influence. The splenic flexure cases have some of the cardinal signs and symptoms of the NCA group, such as sighing respiration, fatigue, palpitation and pain and tenderness over the fourth and fifth left costochondral junctions[1,2].

A more subtle aspect of the irritable colon syndrome is its relationship to disturbances of the cardiovascular system. It is difficult to diagnose gastrointestinal disease manifested by pain or bloating. It is more difficult to diagnose cardiovascular symptoms secondary to irritability of the colon when there is no symptom awareness of the gastrointestinal disturbances. Most usually this involves patients in the older age group who have considerable cerebral and coronary arteriosclerosis. These patients complain of fainting, weakness, dizziness, biliousness, spots before the eyes. It is easy to attribute these symptoms to organic brain disease. If the symptoms are episodic and severe enough, it is easy to attribute them to primary spasm of cerebral vessels. Often these patients are suffering from an irritable colon, but are not aware of this. They must be asked leading questions and then they will remember that they are often bloated, that they have had "spastic constipation". These are the ones who develop diverticulosis, after a long history of spasticity, weakening of the colon wall, and secondary outpouching. Biliousness, as a presenting symptom, should awaken the physician's search for irritability of the colon. Even though the word is used in different sense by many people to refer to their general malaise and dizziness, they have some underlying hunch that "indigestion" is behind it. Of course, it is easy to think of a diseased gallbladder. Search for gallstones in this age group will give numerous positive studies, but this may be misleading. A larger percentage exhibit the irritable colon syndrome. Physiologically, the cerebral symptoms such as dizziness and fainting are based on autonomic imbalance. With the increased vagus discharge to the colon, there is slowing of the heart rate, with drop in cardiac output. This fall in cardiac output is the probable basis for the cerebral symptoms. It is very similar to primary shock or simple fainting. The hands and feet are cold, the forehead is clammy. Prominent anxiety may cause a mixed picture with the sympathetics effecting a change in cardiac output through increase in rate. It is remarkable how much help can be given such a patient by use of a sedative, a wise diet, and insight. These simple measures control many of these problems. It is certainly better to take a positive approach in treating the cases labeled as cerebral arteriosclerosis, than the negative attitude of thinking that these narrow vessels cannot be reopened, and therefore, there is no aid possible for the patient.

Another symptom of the irritable colon that can be a clue is marked weakness. These patients state that they are weak to their fingertips, have no strength; they feel their blood pressure is low. Many of them have been told that they do suffer from low blood pressure. NCA's and other anxiety states

also show similar weakness due to autonomic imbalance or subconscious tightening of voluntary muscles.

The heart with advanced arteriosclerotic change, can also be involved in similar way by the irritable colon when associated autonomic imbalance causes decrease in cardiac output and change in pulse pressure. This decrease in cardiac output may be due to a vagus effect with slowing of the heart, fall in pressure and coronary insufficiency. Here again, anxiety and its sympathetic effect may overshadow the vagus and cause rapid heart beat with the same result.

Many of these cases with cardiovascular symptoms, who have hidden irritability of the colon, often are indiscreet with their diets. It is surprising how much coffee these people drink, and how often they like food delicacies to brighten up their meals, even though they are aware that these delicacies are difficult to digest. These patients will deceive themselves about what they are eating. It is usually the spouse who will give them away. Once we have set in motion a *normal* dietary regime, we can gradually force the patients to become aware of their indiscretion. Only then, with understanding, will they first realize they have been having colonic symptoms, these having been overshadowed in their mind by symptoms referred to the brain and heart.

Another clue to the presence of indigestion in old people, who complain of various cardiovascular symptoms, is afforded by a leading question concerning the taking of soda or its equivalent with meals. This has become a habit of long duration, of which they are no longer aware. It is an indication of the long-standing unheeded indigestion. While on the subject of use of soda for the bloating due to an irritable colon, I must raise the interesting question of why soda is so successful. Perhaps, I should ask, "Why should an abdomen full of gas be aided by the addition of more gas". My interpretation is that the adding of gas to the stomach sets off a gastrocolic reflex, which breaks up areas of spasm and allows for the redistribution of gas in the intestinal tract. I have always felt that bloating, due to the irritable colon, is not alone due to air swallowing or other complicated mechanisms; rather it is due to bunching of the gas in a colon and intestine, dotted by small areas of spasm. This would be similar to the improper packing of a valise. Rearrangement of contents, by making better use of the volume, can often allow a valise to close very readily. The gastrocolic reflex set off by the liberation of carbon dioxide in the stomach, sets off peristaltic waves, which seem to temporarily allow the intestine to overcome its irritability. Thus, the colonic contents spread out in a more equitable distribution throughout all the loops rather than being bunched in certain areas.

One other possible mechanism for further explanation of the cerebrovascular changes associated with the irritable colon, concerns itself with the vagovagal reflex. Such a reflex could be initiated when the colon has a peristaltic wave reaching an area of spasm. The distention of the colon proximal to the spasm,

in the attempt of the peristaltic wave to carry its contents past the narrowed area, increases the vagus effect by such a vagovagal reflex. Thus, there would be two mechanisms for the marked vagal effects – one would be the hypervagotonia that is caused by the autonomic imbalance associated with the basic emotional force, the second would be further vagal discharge through distention of the colon, as just brought out. In addition to the influence of emotional reaction, further aggravation can be attributed to use of irritating foods or drinks. This explains why one or two bites of food can cause bloating. In these instances the stomach is irritated as by coffee or pepper. The resulting gastrocolic reflex is not physiological as it is with soda and carbon dioxide; rather it is probably a more violent gastrocolic reflex with further aggravation of the spasticity of colonic areas.

Conclusion

Today's physician and students must take advantage of knowledge that has been suspected by physicians and philosophers through the long centuries of history. From ancient days it has been stressed that the patient should be treated as entity. There is no separation of the mind from the body. Today we know that in this "age of anxiety", from our psychiatric discoveries and the physiological explanations of the autonomic nervous system, every human being expresses physiological changes throughout his body with each emotional experience; each action of each individual is colored by emotions; therefore, there is constant dynamic body change going on at all times. Until society changes some of the environmental forces, most all of our citizens are exposed to forces that set up enough emotion with secondary physiological body change so that each is heir to the organic disturbances which are so extensive today. This can better be expressed in the words of a patient who came to me with a bleeding peptic ulcer. When I told him the diagnosis, he said he was relatively lucky. I thought he was unusually euphoric until he offered the following explanation. He was an executive with an oil company and stated that, "In my office, executives leave in one of four ways. They either develop high blood pressure and have strokes or they have heart attacks, bleeding ulcers or become alcoholics". He concluded by asking me which of the four I considered preferable. I think that his logic was good. He did have the best of the four diseases, because he would have a better chance than the others to readjust himself.

Emotional reaction involves a diffuse set of body symptoms which may give emphasis to one particular organ system. One of the most common organ systems involved is the large intestine. We have tried to show that direct explanation of colonic symptoms has not been fully made known, that there are several syndromes which will be worked out by clinicians in the years to come. We have further tried to show that there may be numerous instances of secondary involvement of the cardiovascular system without the awareness of the role of instigation played by the irritable colon. The explanation of all

symptoms involved is not easy, as emotional forces express themselves not only through increased vagus influence, but also through the sympathetic and voluntary system. We must constantly try to define the physiological basis for symptoms so that we can improve our understanding and also help our awareness of the entire patient involved in illness.

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Discussion

Dr. William W. Abrams (Kansas City, Kans.):—There are some of us here in the audience who recall that about a year or two ago an essayist spoke on air-swallowing as a cause of abdominal distress. Besides mentioning the considerable work of others on this subject the speaker showed films of an isotope-tagged air bolus that appeared in the rectum in about ten minutes after swallowing the air.

As to anticholinergic nonspecificity, I wish to state a divergence of opinion on this subject has existed for years. More than 30 years ago anticholinergic properties were attributed to belladonna and it was felt that it was the atropine (in the belladonna) that had a specificity for the upper gastrointestinal system, heart and lungs. Inhibition of the upper vagal distribution was the action described.

On the other hand, the alkaloids hyoscine and hyoscyamine (in hyoscyamus) had a specificity for the lower gastrointestinal system and the genitourinary system.

Recently there have appeared in our medical armamentarium many synthetic drugs with selective anticholinergic action for upper gastrointestinal tract diseases, as well as for lower gastrointestinal and genitourinary diseases.

Dr. O. H. Wangensteen:—Dr. Halle's presentation obviously is not an easy subject to discuss. Dr. Halle is painting on a big, wide canvas. In his strenuous efforts to put a splash here and there on his creation, he lost me after one of the first alcoves on his attempts to weld together a number of conditions, which, to my way of thinking, have no direction or relationship to one another.

We have had the opportunity of hearing some very interesting and novel physiological ideas this afternoon. Dr. Snapper mentioned colectomy. A famous surgeon in London, by the name of Sir Arbuthnot Lane at Guy's Hospital, addressed the Royal Society of Medicine many years before he gave up colectomy; when his hospital positions terminated, he found Petrolagar useful in the very same diseases for which he had previously advocated colectomy. In a discussion which took place at the Royal Society of Medicine meeting following a presentation of Sir Arbuthnot's on colectomy, for conditions such as constipation, epilepsy, exophthalmic goiter, and other similar indications, one of the discussants is said to have spoken much as follows—a story repeated to me somewhat more than 30 years ago by someone present at the discussion.

Said Sir Arbuthnot's critic: "Sir Arbuthnot certainly does the operation of colectomy superbly and skillfully; in fact, continued the critic, "it reminds me very much of the squirrel running up and down a tree. He does it with grace and elegance, but why in hell he does it, one will probably never understand." I suspect some of the things of which Dr. Halle told us are a bit like that.

Now, when Dr. Halle talks about sigmoiditis, or spasm in the colon, diverticulosis and diverticulitis, I believe I can understand him; however, I would be inclined to put a somewhat different interpretation upon his observations. I would say that the symptoms of spasm in areas, which the roentgenologist observes—that these are probably occasioned by the diverticula going through the process of herniation of the mucosa, through the blood vessel aperture in the muscle wall of the bowel. I find it very difficult to believe that a cultivated control of emotional restraint is going to keep that from happening. After all, a propensity to colic diverticula is an endowment that comes from nature.

It is like this: these diverticula occur where the mesenteric arteries enter the muscle wall of the bowel. They may occur in the colon in four areas. They perforate the bowel wall at one and five o'clock and again at seven and eleven o'clock.

The distinction between diverticulosis and diverticulitis is an artificial one. Presently a number of us are going to take courage and say these are simply different stages of the same disease. A patient who has colic diverticula and has symptoms has diverticulitis. Why not call it diverticulitis? Surgeons, as you know, have been resecting the colon for diverticulitis, now for some time. In fact, it is just 15 years since I began advocating primary resection for diverticula accompanied by symptoms [*Surgery* 14:403-432 (Sept.), 1943].

How does obstruction and perforation come about in the presence of colic diverticula? And what causes hemorrhages? My feeling is that obstruction is a consequence of perforation in which a localized abscess has formed. Hemorrhage is probably a result of torsion or injury to the blood vessel when the colic

mucosa prolapses through the aperture in the muscle wall of the bowel through which the artery reaches the mucosa.

I am familiar with what Dr. Halle has described in the cecum. A number of papers have been written about this and every once in a while, I think I see this phenomenon. What it is, I do not know, or what makes it I do not know.

Ever since Heberden (1783) first described angina pectoris a number of ailments, accompanied by chest pains, have been badly mislabeled. Michael Herrick of Chicago (1913) brought the problem of coronary thrombosis into sharper focus by his lucid description of the disease. Yet, even now, in 1958, we are diagnosing patients with coronary disease who do not have it. Even electrocardiographic evidence can be misleading. The work of my colleague, Dr. Alan Thal, suggests that in many instances an angiogram is necessary for the diagnosis of coronary-heart disease.

Dr. Halle, I think, is a very courageous man to try to put the many facets which he has been discussing into one package, or, as he implies, that all these diseases stem from a spastic colon. If anyone has that much trouble with his colon, why not get rid of the colon? But I would be afraid that the patient who got rid of his colon for some of the conditions which Dr. Halle has described, unless it were for diverticulosis or diverticulitis, which I think are pretty much the same disease, that these patients would probably have some new symptoms. I hope that Dr. Halle will continue to dissect and probe this problem. It is a very complicated one, and we would all welcome some good factual knowledge of how these disease entities come about.

As the last speaker, Dr. Abrams, remarked, gas in the intestinal canal is largely swallowed air. My colleague, Dr. Charles Rea and I, 25 years ago, divided the cervical esophagus in a dog's neck and obstructed the distal ileum. We then closed the distal end of the divided cervical esophagus and observed that some of our dogs lived for seven weeks or more. At autopsy there was no distention of the intestine—just a little amorphous lump in the colon, proximal to the occlusion. This simple experiment demonstrated that swallowed air is the chief source of intestinal distention.

If one places the tip of a duodenal tube into the duodenum and injects barium into the duodenum, the barium often will be observed to reach the cecum in ten minutes. The greatest time lapse, of course, is required for passage of the barium from the stomach. That may take a long time, but once in the duodenum it takes but a few minutes for it to reach the colon. In an infant with a normal alimentary canal, one will see that air reaches the rectum usually within 14 hours after birth.

The subject which Dr. Halle has been exploring is indeed a fascinating one, but he has yet to find the proper handle by which to seize the problem to shake it down properly.

Dr. I. Snapper:—Dr. Halle has brought back many of my old friends who nearly have been forgotten. First of all, he reminded us of Metchnikoff who ascribed the longevity of the Bulgarians to the addition of yogurt to their daily diet. This nutrient changes the flora of the intestine and this in Metchnikoff's opinion was a major factor for the longevity of the Bulgarians. The English surgeon Arbuthnot Lane was even more radical than Metchnikoff. He removed the colon in many different diseases in order to cure the pernicious influence of the bacteria in the colon on the human organism.

Dr. Rumheld, 40 years ago, described the "splenic flexure syndrome" with pains in the epigastrium radiating to the left shoulder and considered this the etiology of a syndrome which most of us diagnosed as coronary insufficiency.

The influence of the parasympathetic nerve centers on the function of stomach and intestine has been well known for more than half a century. In the last years of the nineteenth century Dr. Talma, Professor of Internal Medicine at Utrecht, stimulated the peripheral stump of the transsected vagus nerve in rabbits and thereby caused ulcers of the stomach.

This vagus stimulation caused a spasm of the muscularis mucosae which obstructed the blood vessels and the ensuing anemia allegedly led to ulcer formation.

In my time nobody took Talma's concept seriously and we had to wait until Dr. Dragstedt resected the vagus nerve in humans and demonstrated the favorable influence of this procedure on the course of peptic ulcer in humans.

We will all agree that the intestine suffers in cardiac congestion; as a matter of fact, the very first signs of venous hypertension in the intestinal wall is meteorism.

Clinicopathological Conference*

from the Touro Infirmary, New Orleans, La.

Dr. Carl J. Tripoli:—Gentlemen, we will call the meeting to order, and the program will begin with Dr. Hertzog, who is the chairman of this presentation. As you know, Dr. Ambrose J. Hertzog, of New Orleans, is Lecturer in Pathology, at Tulane University, and also Director of the Laboratories and Chief Pathologist at Touro Infirmary here in New Orleans.

Dr. Ambrose J. Hertzog:—Thank you, Dr. Tripoli.

I think we are very fortunate to have Dr. I. Snapper, Director of Medical Education, Beth El Hospital, Brooklyn, N. Y. and Dr. Owen H. Wangensteen, Professor and Chairman, Department of Surgery, University of Minnesota Medical School, Minneapolis, Minn., here with us. They need no introduction, and without further ado I think we should start the meeting on this first case which we will ask Dr. Snapper to discuss.

PROTOCOL—I

This 31-year old white female, a native of New Orleans, had 13 admissions to Touro Infirmary since the age of 14 years. She was first seen on 13 August 1940 complaining of nose bleed and bleeding from gums for past 6 months. There was no family history of bleeding. One brother had tuberculosis; another hepatitis; and father had tuberculosis and diabetes. She had been running a low grade fever. Pertinent findings were those of a poorly developed young girl with a greatly enlarged spleen. Bleeding and coagulation times were normal as well as platelet counts and tests for capillary fragility. Prothrombin time was 68 per cent of normal. X-ray of chest showed a slight prominence of the pulmonary artery. Blood picture was that of hypochromic microcytic anemia of 2,720,000 red cells. Fragility test was normal. On 9 September 1940 a splenectomy was done with removal of a 550 gm. spleen. Histologically the spleen showed "chronic splenitis with fibrosis and hemosiderin deposits". She had a postoperative pneumonia. She was discharged on 9 September 1940 with diagnosis of Banti's disease.

She was readmitted on 4 December 1940 complaining of fever with sore throat and had been coughing up clots of dark blood with frequent nose bleeds. Physical examination revealed nasal mucosa to be congested with tendency to bleed. Tongue was not abnormal and mucous membranes of mouth were very red. There was an unexplained cervical adenitis. She ran a septic fever and was

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discharged as improved on 20 December 1940. Red cell count varied from 4,050,000 to 3,200,000.

She was readmitted on 24 September 1941 because of a continuous low grade fever. A chest x-ray was negative. There was no adenopathy this admission. Physical examination was negative except for presence of spider angiomata over the upper trunk and arms, bleeding carious teeth, and an enlarged heart with a systolic aortic murmur. Agglutination tests were positive for B. Abortus (1/800). Blood cultures were negative. Hemoglobin was 65 per cent with 3,325,000 red blood cells; leucocyte count was 6,500 with 59 per cent lymphocytes. She was discharged on 19 October 1941 with diagnosis of undulant fever.

She was readmitted on 2 March 1942 complaining of a cough with blood tinged sputum and fever of one week's duration. Mucous membranes of mouth revealed numerous hemorrhagic areas. Oral hygiene was poor. Liver was enlarged and palpable 2 fingers below costal margin. Cephalin flocculation test was 2 plus and prothrombin level was 48 per cent. Hemoglobin was 60 per cent and red cells were 3,400,000. Leucocyte count was 14,500 with 92 per cent neutrophils. Clinical diagnosis was cirrhosis of liver.

She was readmitted on 16 March 1943 complaining of bleeding gums. The gums appeared to have retracted from the teeth and were tender to pressure. Bleeding and coagulation times and platelet counts were normal. RBC 2,600,000 and hemoglobin was 4.75 gm. She was referred to dental clinic for a tooth extraction. Following extraction, she bled profusely and was readmitted to the hospital. In October of 1943, three more teeth were extracted and she was again readmitted for bleeding from the mouth. Physical examination revealed profuse bleeding from the sockets. There was a soft systolic murmur at the pulmonic and aortic areas of the heart. Marked clubbing of the fingers was noted. Hemoglobin was 62 per cent and red cells were 3.45. Clinical diagnosis was possible congenital heart diseases.

She was readmitted on 14 August 1944. She had been fairly well and had worked as a clerk in a downtown department store. She still suffered from periodic spontaneous nose bleeds. She looked pale but lips were red. Physical examination revealed a pale undernourished girl of 18 years complaining of pain in the upper left quadrant of the abdomen. There were telangiectatic spots over the skin of the arms, chest, back and arms. There was marked clubbing of the fingers of both hands with a suggestion of clubbing of the toes. The lungs were negative. The liver did not appear enlarged. The heart appeared enlarged to the left with a slight systolic thrill over the apex and a systolic murmur at the apex. Fluoroscopic examination of the chest revealed no abnormality. A gastrointestinal x-ray study was negative. X-rays of chest showed no evidence of pulmonary disease. Hemoglobin was 25 per cent with 2,500,000

red blood cells. Serology was negative. A muscle biopsy was noncontributory. She was discharged on 23 August 1944 as an undiagnosed disease.

She was readmitted on 17 April 1950 with chills and fever and x-ray evidence of pneumonia. She was emaciated, cyanotic, with marked clubbing of fingers and toes. There was a systolic murmur at all valve areas. Temperature was 103 degrees. She was discharged on 6 May 1950 when all studies and consultation yielded a final diagnosis of juvenile cirrhosis of the liver with superimposed infections from time to time.

The patient was improved and worked in a doctor's office. She was readmitted on 25 February 1957 and 9 October 1957 because of epigastric pain and melena. In August of 1957 she had a cardiac catheterization done at another hospital and multiple diffuse pulmonary arteriovenous fistulas were thought to be present. Hemoglobin was 10 gm. and red cell count was 3,710,000. Leucocyte count was 7,000 with 54 per cent lymphocytes. Platelets were 214,110. Cephalin flocculation test was 2 plus. Bilirubin was 0.26. Alkaline phosphatase was 6.6 units. NPN was 32. Glucose was 125. Total protein were 5.7 gm. with 3.0 gm. albumin and 2.7 gm. of globulin. She was discharged with diagnosis of multiple A-V fistula of lungs. An ECG was normal and a chest x-ray showed only prominent vascular markings.

Her last admission was on 15 December 1957 complaining of abdominal pain, hematemesis, melena, and jaundice. A gastrointestinal x-ray series demonstrated esophageal varices. There was evidence of ascites. A Sengstaken tube was inserted. She received multiple blood transfusions and expired on 15 December 1957.

Dr. I. Snapper:—Mr. Chairman, Dr. Hertzog, Ladies and Gentlemen: This first case concerns a 31-year old white woman, a native of this city, who had 13 admissions to Touro Infirmary between 1940 and 1957. She was first seen on 13 August 1940, when she was 14 years old, complaining of nose bleeds and bleeding from the gums for the past six months. There was no family history of bleeding.

One brother had tuberculosis, and it is therefore possible that she also had tuberculosis, especially because she had been running a low grade fever. This brother also had hepatitis, which is not a familial disease. The father had tuberculosis and diabetes. The diabetes of the father is of little importance to the children because children of a diabetic father and a healthy mother do not suffer more frequently from diabetes than children of a healthy couple.

Pertinent findings were those of a poorly developed young girl with a greatly enlarged spleen. There is a long list of diseases in which the spleen may be enlarged. In this case we are in a favorable position, because the spleen was removed and the histologic examination permits exclusion of many diseases which may cause an enlarged spleen.

The bleeding and coagulation times were normal as well as platelet counts and tests for capillary fragility. The prothrombin time, however, was increased and the prothrombin content of the plasma was only 68 per cent of normal.

X-ray of the chest showed a slight prominence of the pulmonary artery which usually indicates that the right ventricle is hypertrophic.

The blood picture was that of a hypochromic microcytic anemia with 2,720,000 red cells. Fragility test was normal. The presence of hypochromic microcytic anemia indicates a disturbance of the iron metabolism. Either the patient doesn't absorb iron sufficiently, or—which nowadays is extremely rare—the patient doesn't receive enough iron in his food, or the patient is losing iron by hemorrhage. Later we will see determinations of hemoglobin and red cells which will not indicate a hypochromic microcytic anemia. It is evident that since she had nose bleeding and bleeding of the gums, she may well have had a hypochromic microcytic anemia at this time.

Again, the fragility test was normal. On 9 September 1940, a 550 gm. spleen was removed. Histologically the spleen showed "chronic splenitis with fibrosis and hemosiderin deposits". She had a postoperative pneumonia. She was discharged on 9 September 1940 with a diagnosis of Banti's disease.

Banti was a professor of internal medicine at Florence. He described a disease which was characterized by the presence of anemia and splenomegaly. Later these patients developed cirrhosis. Histologically the disease which Banti described was characterized by a special fibroadenie of the spleen i.e. fibrosis surrounding the central arteries of the Malpighian bodies of the spleen.*

The pathologic report of the spleen of our patient does not mention any periarterial fibrosis. Therefore, so far as this report is concerned, we should not speak of Banti's disease.

Nearly all pathologists are of the opinion that the disease of the spleen, Banti described, does not exist. The famous Eppinter, at the time professor of medicine in Vienna, however, traveled to Florence and studied the original slides of Banti, in which to his surprise he actually found fibrosis around the central arteries of the Malpighian bodies. He, therefore, once more examined very carefully every case of splenomegaly that came to him and discovered the true histologic lesions of Banti's disease in the enlarged spleen of a young man who had been born in Albania. He then concluded that Banti's disease does occur in Northern Italy and in certain countries on the coast of the Adriatic Sea, but probably not in other parts of the world. The possibility that all these patients may have had *lupus erythematosus* with liver damage has perhaps to be considered!

*At this point lantern slides of the original microphotos Banti published were projected.

Our patient of today who had suffered from a splenomegaly but certainly not from Banti's disease was admitted again three months later, complaining of fever with sore throat. She had been coughing up clots of dark blood with frequent nose bleeds. At the previous admission she had suffered from epistaxis and bleeding gums, now in addition to nose bleeding, she is coughing up clots of dark blood. Physical examination revealed a congested nasal mucosa with a hemorrhagic tendency. This could *perhaps* be caused by the hypothrombinemia which had been present at the first admission. The tongue was not abnormal but the mucous membrane of the mouth was very red. There was an unexplained cervical adenitis. She ran a septic fever and was discharged as improved some two weeks later.

She was readmitted in September of 1941, nine months later with a continuous low grade fever. A chest x-ray was negative. There was no adenopathy at this admission. Physical examination was negative except for the presence of spider angiomata over the upper trunk and arms, bleeding carious teeth, and an enlarged heart with a systolic aortic murmur.

Here semantics are all important. A spider angioma is a specific angioma with a central, thick-walled giant arteriole which branches out into many smaller thick-walled arterioles. The latter connect with venules and capillaries. The central arteriole is so muscular and its pulsations so strong that the spider angioma is pulsating in character. In the presence of pulsating spider angiomata the diagnosis of liver cirrhosis is in order.

I must now already mention that later in the history other angiomas were mentioned which are not spider angiomata. Actually this patient therefore had two different kinds of angiomas.

The spider angiomata were spread over the upper part of the trunk and arms. In addition bleeding carious teeth, and an enlarged heart with a systolic aortic murmur were found. Agglutination tests were positive for B. Abortus (1/800). Blood cultures were negative. Hemoglobin was 65 per cent with 3,325,000 red blood cells, which is a normochromic anemia. The latter cannot be due to blood loss but may well be connected with a liver insufficiency.

The leucocyte count was 6,500 with 59 per cent lymphocytes. She was discharged on 19 October 1941 with a diagnosis of undulant fever.

Is undulant fever endemic here?

Dr. Hertzog:—No, we only see an occasional sporadic case, usually in a patient from outside New Orleans.

Dr. Snapper:—She was readmitted on 2 March 1942 complaining of a cough, again with blood-tinged sputum and fever of one week's duration. Mucous membranes of the mouth revealed numerous hemorrhagic areas. Oral hygiene

was poor. The liver was enlarged and palpable two fingers below the costal margin.

The cephalin flocculation test was 2+, and the serum prothrombin level was 48 per cent. The cephalin flocculation test result must be considered to be within normal limits, but the repeatedly low prothrombin level indicates that she actually has liver insufficiency. The hemoglobin was 60 per cent and red cells were 3,400,000. The leucocyte count was 14,500 with 92 per cent neutrophils.

Liver cirrhosis in children does occur but not too frequently, and we will have to find a special reason why this child had a liver cirrhosis.

She was readmitted on 16 March 1943, complaining of bleeding gums. The gums appeared to have retracted from the teeth and were tender to pressure. Bleeding, coagulation times and platelet counts were normal. Red blood count was 2,600,000, and the hemoglobin was 4.75 gm. again a hypochromic anemia probably due to blood loss. Following extraction she bled profusely, which was to be expected in view of the hypoprothrombinemia, and was readmitted to the hospital.

Seven months later, in October of 1943, three more teeth were extracted and she again had to be admitted for bleeding from the mouth. Physical examination revealed profuse bleeding from the sockets. There was a soft systolic murmur at the pulmonic and aortic areas of the heart. Marked clubbing of the fingers was noted. Clubbing of the fingers does occur in liver cirrhosis, though it is relatively rare. The hemoglobin was 62 per cent and red cells 3,450,000, slightly hypochromic. A clinical diagnosis was made of a possible congenital heart disease.

She was readmitted on 14 August 1944. She had been fairly well and had worked as a clerk in a downtown department store. She still suffered from periodic spontaneous nose bleeds. She looked pale but her lips were red. Physical examination revealed a pale, undernourished girl of 18 years, complaining of pain in the upper left quadrant of the abdomen. There were telangiectatic spots over the skin of the arms, chest, and back.

Telangiectasias, i.e. skeins of thin-walled arterioles should be distinguished from spider angiomata.

We, therefore, must conclude that this patient had both spider angiomata and telangiectasias. In the presence of the latter angiomas, the diagnosis of familial hemorrhagic telangiectasia, Osler-Weber-Rendu's disease is in order.

Familial telangiectasia is not a disease which only hits the small arterioles of the skin and mucous membranes. At the same time other organs may be involved; especially enlargement of the liver due to Laennec's cirrhosis frequently occurs.

In the Swiss literature it is generally accepted that a patient in whom both telangiectasia and spider angiomata are present, is suffering from a combination of liver cirrhosis and Osler's disease. In the American literature the liver enlargement present in hereditary telangiectasia is often ascribed to angiomatosis of the liver.

Since the patient of today had spider angiomata two years ago and telangiectasia now, she must have familial hemorrhagic telangiectasia and the large spleen and liver must then be due to cirrhosis of the liver.

The family history does not mention spontaneous bleeding in her siblings or parents and she must, therefore, belong to the 20 per cent of patients with familial telangiectasia without clear-cut familial history. There may of course, have been a grandfather, or a great-grandmother who suffered from this disease which then has skipped a few generations.

She is relatively young to have signs and symptoms of it because in most patients with Osler's disease the hemorrhage from the telangiectases starts when the patients are about 20 years of age. The first signs in our patient started already when she was 14 years of age.

The protocol mentions not only telangiectatic spots over the skin of the arms, chest and back, but in addition marked clubbing of the fingers of both hands with a suggestion of clubbing of the toes. Clubbing, as mentioned before, could perhaps be connected with the liver cirrhosis. In the presence of the telangiectasia, however, the clubbed fingers probably must be explained differently.

The lungs were negative. The heart appeared enlarged to the left with a slight systolic thrill over the apex and a systolic murmur at the apex. Fluoroscopic examination of the chest revealed no abnormality. A gastrointestinal x-ray study was negative. X-rays of the chest showed no evidence of pulmonary disease. Hemoglobin was 25 per cent with 2,500,000 red blood cells. Serology was negative. A muscle biopsy was noncontributory. She was discharged on 23 August 1944, with an undiagnosed disease.

She was readmitted 17 April 1950, with chills, fever and x-ray evidence of pneumonia. She was emaciated, cyanotic, with marked clubbing of fingers and toes. For the first time we hear about cyanosis. There was a systolic murmur at all valvular areas. The temperature was 103 degrees. She was discharged on 6 May 1950, when all studies and consultation yielded a final diagnosis of juvenile cirrhosis of the liver with superimposed incidental infections.

The patient improved and worked in a doctor's office. She was readmitted 25 February 1957 and 9 October 1957, because of epigastric pain and melena. In August of 1957, she had a cardiac catheterization done at another hospital

and multiple diffuse pulmonary arteriovenous fistulas were thought to be present.

These data actually complete the clinical picture because one-third of the patients with arteriovenous aneurysms of the lungs have Osler's disease.

Hemoglobin was 10 gm. and red cell count was 3,710,000. Leucocyte count was 7,000 with 54 per cent lymphocytes. Platelets were 214,110, cephalin flocculation test 2 plus, bilirubin 0.26, alkaline phosphatase 6.6 units, NPN 23, glucose 125, total protein 5.7 gm. with 3.0 gm. albumin and 2.7 gm. of globulin. She was discharged with a diagnosis of multiple arteriovenous fistulas of the lungs. An electrocardiogram was normal and a chest x-ray showed only prominent bronchial markings.

The last admission was on 15 December 1957, for complaints of abdominal pain, hematemesis, melena, and jaundice. In liver cirrhosis the development of jaundice usually indicates that the patient is going to die soon because acute and extensive damage of liver tissue is superimposed on the Laennec's cirrhosis. A gastrointestinal x-ray series demonstrated esophageal varices. There was evidence of ascites. A Sengstaken tube was inserted,—another ominous sign predicting that a fatal ending is approaching rapidly. She received multiple blood transfusions, and died on 15 December 1957.

Summarizing this somewhat complicated history it is certain that this patient had hemorrhagic telangiectasia combined with portal hypertension, due to a juvenile cirrhosis. The hemorrhagic telangiectasia explains hemorrhage from gums and bronchi, the liver cirrhosis is the cause of the esophageal hemorrhage. Finally there were—as is often the case in Osler-Weber-Rendu's disease—arteriovenous fistulas in the lungs, leading to clubbing of the fingers and toes.

A juvenile cirrhosis is usually a cholangiolitic cirrhosis.

Now we have to make a few diagnostic acrobatics to explain why, in this case the arteriovenous fistulas of the lungs did not cause cyanosis. Cyanosis can be expected when the arteriovenous fistulas represent communications between the pulmonary artery venous blood and the pulmonary veins (arterial blood). In the absence of cyanosis communications between the *bronchial* artery and the pulmonary veins may have been present. In such a case arterial blood of the bronchial artery is mixed with the arterial blood of the pulmonary veins. This may be the reason why our patient has hardly ever been cyanotic.

Well, Dr. Hertzog, you will have to agree that I have stuck out my neck, farther and farther, until it could not be stretched anymore.

Question:—Were there any studies of bone and skeletal system? Were there any changes, like a syndrome?

Dr. O. H. Wangensteen:—I see nothing about the heart and blood vessels. They may be withholding that.

Dr. Snapper:—The child had a low blood pressure, maybe because she had chronic anemia.

Dr. Wangensteen:—Undulant fever?

Dr. Snapper:—She may well have had undulant fever but "this has nothing to do with the case". The arteriovenous fistulas and the anemia explain the presence of an enlarged heart.

Dr. Hertzog:—Dr. Snapper made the diagnosis much easier than we did at autopsy. I should like to ask Dr. Wangensteen to make a comment.

Dr. Wangensteen:—I do not believe this case comes into my area of interest. I admit to having become lost in the maze of things that Dr. Snapper discussed and I believe he was on the correct scent. I have in mind there may have been an associated cardiac lesion, an aortitis, or of valvular heart disease as a consequence of undulant fever.

Dr. Frank J. Borrelli:—Will you please comment on the advisability of surgical procedures in this instance?

Dr. Wangensteen:—I have read some of Banti's papers of the 1910-12 era. I saw the name of Banti on a cement sidewalk block in the courtyard approach to the Municipal Hospital in Florence somewhat more than 30 years ago. Banti had only died a few years before in 1925. Banti's first papers on Splenic Anemia appeared in 1894. He called the condition Splenomegaly with hepatic cirrhosis. It was Banti's friends and associates who gave splenic anemia the eponym, Banti's Disease.

Professional pathologists commenced with Rokitansky and Virchow. Samuel D. Gross (1839) made the first attempt to write a systematic pathology, poised of course toward surgery. Banti, though primarily a pathologist had his own wards and had therefore more than an ordinary concern in the clinical aspects of diseases in which he had a special interest. In fact, I believe he did his own splenectomies around the turn of the century. A very interesting biography has recently been written of Banti in Scientia Medica Italica (7:13, July-September, 1958).

The observations of Rousselot, Whipple, and their associates, suggesting the presence of an extrahepatic block in the portal vein, as the primary cause of splenomegaly in Banti's disease, have succeeded in shifting considerably the emphasis concerning the nature of Banti's splenic anemia. Today, it is generally regarded as a primary portal hypertension secondary to a cavernoma in the portal vein, which in turn may trace to an infantile thrombophlebitis of the umbilical veins, at least in some cases.

I have removed spleens for a large variety of reasons. In Minnesota, our pathologists call what has been commonly known as Banti's disease, fibrosis of the spleen, or splenomegaly owing to an extrahepatic block of the portal vein.

I see Dr. Rives is here. He is a surgeon expert in problems of the spleen, and I do not want to say anything more, for I know you would prefer to hear something concerning technics of splenectomy directly from him. The Banti spleen is invariably large and adherent, making its removal difficult. There is great thickening of all the peritoneal membranes, which in turn is probably a reflection of increased portal pressure. When the portal pressure is normal, the peritoneal membranes are thin and diaphanous. In the presence of portal hypertension, all abdominal operations are difficult and take a long time—perhaps three times as long as the surgeon anticipates, because of the bleeding from all peritoneal surfaces.

Blakemore, I believe, states it is unnecessary to take out the spleen for the portal hypertension in patients in whom it is possible to do a portacaval shunt. Blakemore finds that an effectual portacaval shunt will reduce the portal hypertension, in consequence of which the spleen will automatically become reduced in size, and the hypersplenism of the so-called Banti's syndrome will disappear.

Dr. Snapper:—It is quite evident that there are many other possibilities. She may well have had an extra lobe in the lung.

As far as the heart is concerned, personally I thought that all of the signs of the heart were explained by arteriovenous aneurysms of the lung, the repeated hemorrhages and the long standing anemia. Apart from all this she may also have had a terminal thrombotic endocarditis.

But I say the latter only to satisfy my friend Owen.

Dr. Hertzog:—We have about 45 minutes left and we have another case, so we had better go right along without any further discussion of this case.

I will show you the x-rays of this case. Apparently she had no cardiac enlargement and nothing to resemble an arteriovenous aneurysm of the lung.

(Slide) This is an angiocardiogram, which was normal. A diagnosis of a pulmonary arteriovenous shunt was made by exclusion. She had a low oxygen tension in the peripheral blood and it was postulated she must have a mixture of venous and arterial blood. These studies were made at the Ochsner clinic.

(Slide) A gastrointestinal study was normal except for esophageal varices.

(Slide) This is a picture of the clubbing of the fingers, and the cyanosis which was present. She did have very pronounced clubbing of her fingers.

(Slide) At autopsy, as Dr. Snapper predicted, we found a small 1,100-gm. atrophic hobnail liver with the picture of portal cirrhosis. We did not see anything which resembled an arteriovenous shunt in the liver. I think the terminal pathology which led to her death, was largely hepatic insufficiency, jaundice, ascites, and esophageal varices.

(Slide) There are the esophageal varices, which had ulcerated. At times it is difficult to demonstrate esophageal varices at autopsy because they collapse after death.

(Slide) The lungs grossly appeared normal. We could not demonstrate a saccular aneurysm. The main branches of the pulmonary artery, however, were markedly dilated.

(Slide) The heart weighed 300 gm., which I think was slightly enlarged for a small woman of her size, and it was largely right ventricular hypertrophy. She never had congestive heart failure from her mild *cor pulmonale.*

(Slide) There was an incidental finding of a segmental colitis. These little spots are collections of pus cells. There were also lipomas of the colon. This is something Dr. Snapper didn't diagnose. Lipomas of the colon are not rare in our surgical material at Touro.

(Slide) Microscopically the liver showed a typical picture of a portal cirrhosis in a more or less inactive stage with irregular lobules and interstitial fibrosis. There is nothing here that looks like telangiectasis.

(Slide) Microscopic sections of lung were very illuminating. Almost every section showed large dilated thin-walled vessels with no muscular coat. These vascular spaces were scattered diffusely throughout the parenchyma of both lungs.

(Slide) Whether they represent a connection between pulmonary arterial circulation and the pulmonary veins, or whether they represent bronchial veins, as Dr. Snapper mentioned, I can't answer that question, but I think they do represent a congenital anomaly of these vessels that led to a mixture of arterial-venous blood and resulted in low arterial oxygen pressures as noted in the angiocardiogram study.

Some of these vascular spaces were thrombosed. This was a further load on the right side of the heart.

(Slide) The small arteriovenous shunts were not confined to the lungs.

The capsule of the liver contained these telangiolitic vessels.

(Slide) The pancreas also shows these dilated vessels as well as the kidney.

Dr. James Rives removed the patient's spleen in 1940, and, as Dr. Wangensteen predicted, it showed fibrosis of the pulp with dilated capillaries. This is the microscopic picture of portal hypertension. She may have had portal hypertension independent of cirrhosis of the liver at that time.

Now, as to the anatomical diagnosis. She had Rendu-Osler-Weber's disease. She had multiple small pulmonary arteriovenous fistulas, portal cirrhosis of the

liver, esophageal varices, jaundice, mild *cor pulmonale*, segmental colitis and multiple lipomas of the colon.

As Dr. Snapper mentioned, hereditary telangiectasia is a very old disease, first described by Sutton in 1864 and received the attention of Rendu (1896); Osler (1901); and Weber (1907) by whose names the condition is known.

It is only in recent years that we have begun to recognize that these congenital anomalies of the vascular system in this disease may not be confined to the skin and mucous membranes but may involve the lungs as well as other organs.

Brink, in 1950 called attention to this, and Weiss, in 1954 reported four cases of hereditary telangiectasia with numerous small telangiectases of the lungs which shunted unoxygenated blood. Hales, in 1956 reported two cases with multiple small pulmonary arteriovenous fistulas, and lesions in other organs classified as variants of hereditary hemorrhagic telangiectasia.

In connection with the liver, Fitzhugh, in 1931, reported four cases of telangiectasia with splenomegaly and hepatomegaly, and Smith and Leneback in 1954 wrote an article on hereditary telangiectasia with special reference to hepatic lesions. We can conclude that cirrhosis of the liver is not uncommon in Rendu-Osler-Weber's disease.

How are we going to explain the liver lesions in this syndrome? Several explanations have been given, namely: arteriovenous fistulas in the liver; homologous serum hepatitis from frequent transfusions with complicating cirrhosis, cardiac cirrhosis is secondary to *cor pulmonale;* nutritional deficiency due to protein depletion or poor diets, and other possible causes.

I want to congratulate Dr. Snapper for diagnosing this puzzling case. (Applause). It is quite unusual as it represents a case of Rendu-Osler-Weber's disease with both pulmonary arteriovenous fistulas and cirrhosis of the liver, and prominent clinical findings related to both the lungs and liver. I have not found a similar case in the literature.

Dr. Wangensteen will discuss the next case.

PROTOCOL—II

This 44-year old white female, a housewife and native of New Orleans, was admitted to Touro Infirmary on 22 March 1953, with a history of abdominal pain and rectal bleeding intermittently for the past ten years. Symptoms apparently began following a cesarean section in 1943 in which she began to experience intermittent attacks consisting of bloating in the abdomen and fullness with epigastric burning and anorexia. This progressed to severe cramping in the left abdomen that seemed to involve the entire abdomen. Profuse perspiration was associated. With the onset of abdominal pain there were usually

several soft bowel movements with bright red blood and mucus. Sometimes this gave partial relief of the abdominal cramps. After each attack the rectum seemed to burn for a day or so and the entire attack lasted about 24 hours. Initially attacks occurred every month but during the past year or so they occurred every week or so. Nausea without emesis had been associated.

She began to run a low grade fever. During the interval between attacks gastrointestinal symptoms were very mild, consisting of slight belching and associated epigastric burning. A most recent attack occurred about 20 February 1953 and for the first time was associated with a very profuse watery diarrhea. During the past year she had lost about 12 lbs. At times she ran an intermittent low grade fever.

Systemic review revealed occasional smothering spells with palpitation and skipped "heart beat". There were no urinary symptoms. There was dysmenorrhea and menstrual irregularity subsequent to the first pregnancy. The second and last pregnancy ten years ago was terminated by cesarean section with an uneventful recovery.

Physical examination on admission revealed a well developed, fairly well nourished white female weighing 111 lbs. Temperature was normal. Skeletal structure medium. There was no jaundice. The pupils responded to light and accommodation. Oral hygiene was fair. Most molar teeth were gone. The tonsils were small. The thyroid had a nodular left lobe with moderately enlarged right lobe. The breasts revealed no masses. Blood pressure was 108/80, rate 60. The heart showed split first and second sounds, rhythm regular and no murmurs. Abdomen was flat, with two low middle scars, generalized abdominal tenderness showing no particular localization. Proctoscopic examination revealed rectal tone increased, internal hemorrhoids, a fissure and an anterior pelvic mass painfull on pressure representing probably uterine fibroids. Rectum was clear. The scope was passed to 7 inches, no mucosal lesions were found.

Laboratory studies:—Hemoglobin 13.5 gm. per cent, hematocrit 42, white count 5,200, 58 per cent neutrophils, 37 per cent lymphocytes, 1 per cent eosinophils, 1 per cent basophils, 3 per cent monocytes. Sedimentation rate was 2 mm. Stool examination was negative for blood, ova, cysts and parasites. Gastric analysis (Ewald): pH 3, free HCl 6, total acidity 50 degrees. Wassermann negative. Iodine uptake 10 per cent. Febrile agglutinations for *S typhosus*, H and O antigens, *brucella abortus, brucella proteus* (typhus) and paratyphoid A and B were all negative. Urinalysis—alkaline reaction, specific gravity 1.017, albumin and sugar negative, occasional WBC, occasional epithelial cell on microscopic examination. Basal metabolism on one occasion plus 34, on repeat plus 7.

X-ray studies:—Chest—cardiac silhouette nomal. Lungs clear. Gallbladder—negative for opaque or nonopaque calculi. Gastrointestinal series including small

intestines study—esophagus, stomach and duodenum were negative. There was atypical entering of the terminal ileum into cecum and ascending colon with an atypical redundancy of the ascending colon. Barium enema showed atypical redundancy of ascending colon as mentioned with an area of narrowing at the junction of the descending and sigmoid colons.

Gynecological consultations revealed a cystic enlarged cervix with incomplete stenosis. The fundus was 3 times the normal size with irregular tumor masses. The adnexae were normal. On 26 March 1953 a laparotomy was performed.

Dr. Wangensteen:—It is good to have the opportunity of catching up with my erstwhile colleague, Dr. Hertzog, who for so many years was a member of Dr. Bell's Department at the University of Minnesota. He became quite skilled in the technic of looking back in the records for difficult cases in Bell's Department of Pathology, as is quite obvious in his selection of this case.

My preference is to play the diagnostic problems of the Clinical Pathological Conference by ear rather than by a study of the record.

The story concerns a 44-year old female, a housewife, a native of New Orleans, who was admitted to Touro Infirmary in March of 1953 with a history of abdominal pain and of rectal bleeding which had been intermittent for the past ten years. I think it would be proper to say it could not have been a cancer these ten years.

The symptoms apparently began following a cesarean section in 1943, at which time she began to experience intermittent attacks consisting of bloating in the abdomen and fullness, with epigastric burning and anorexia. These symptoms progressed to severe cramping in the left abdomen and seemed occasionally to involve the entire abdomen. Profuse perspiration was associated. With the onset of abdominal colic there were often several soft bowel movements tinged with bright red blood and mucus.

Sometimes this occurrence afforded partial relief of the abdominal cramps. After each attack the rectum seemed to burn for a day or so, and the entire attack lasted approximately 24 hours. That is a new symptom to me. It may be significant to some of you but it is not especially to me. I suppose the rectal burning might be occasioned by an increased transit rate through the alimentary canal of intestinal content with a low pH. There is, however, no mention of perianal excoriation.

Initially, attacks occurred every month; during the past year or so they have been present every week or so. Nausea without emesis has been associated. Well, every patient with a low grade bowel obstruction involving the terminal ileum does not necessarily vomit. In obstructions of the colon, vomiting, even in the presence of great distention, may be absent.

Our patient then began to run a low grade fever. During the interval between attacks, the gastrointestinal symptoms were very mild, consisting of slight belching and associated epigastric burning. Now, the burning could have been owing to gastric acidity, which in turn could have caused heart burn through relaxation of the gastroesophageal sphincter.

The most recent attack occurred 20 February 1953, about a month before admission to hospital. And for the first time, it was associated with very profuse watery diarrhea. During the last year, she had lost 12 lbs. in weight.

Systemic review revealed occasional smothering spells with palpitation and skipped "heart beat". That is very difficult to interpret; could it have been hysterical dyspnea? Or owing to anemia? A further examination of the record may tell. There were no urinary symptoms. There was dysmenorrhea and menstrual irregularity, subsequent to the first pregnancy. That was in 1943, ten years prior to our current interest in the patient. The second and last pregnancy, ten years ago, was terminated by cesarean section with an uneventful recovery.

Physical examination on admission revealed a well-developed, fairly well-nourished white female weighing 111 lbs. The temperature was normal; the skeletal structure was on medium size. There was no jaundice. The pupils responded to light and accommodation. Oral hygiene was fair. Most molar teeth were gone. The tonsils were small. The thyroid had a nodular left lobe with a moderately enlarged right lobe. The breasts revealed no masses. Blood pressure was 108/80; the pulse rate was 60. The heart showed split first and second sounds; the rhythm was regular and there were no murmurs. Cardiac surgeons are beginning to teach internists and endocardiologists you know, something about the heart and its problems.

The abdomen was flat, with two midline scars; there was generalized abdominal tenderness showing no particular localization. Were there two cesarean sections?

Dr. Hertzog:—There is a record of only one.

Dr. Wangensteen:—Proctoscopic examination revealed increased rectal tone and internal hemorrhoids. There is no reason why an enlarged uterus should be especially tender. I think there must have been something in the peritoneal cavity. Tenderness is a reflection of peritoneal irritation; the most irritating fluid the peritoneum is ever subjected to is the escape of gastric juice, because of its low pH. Blood escaping into the peritoneal cavity also causes some peritoneal irritation, even though the pH is that of blood.

The rectum was clear. The scope was passed to seven inches (almost 18 cm.) and no mucosal lesions were found.

Laboratory studies:—The hemoglobin was 13.5 gm. per cent; the hematocrit 42, white count 5,200; 58 per cent neutrophils; 37 per cent lymphocytes; 1 per cent eosinophils, 1 per cent basophils, 3 per cent monocytes. Sedimentation rate was 2 mm. Stool examination was negative for blood, ova, cysts, and parasites. Gastric analysis (Ewald): pH 3, free hydrochloric acid 6°; total acidity 50°. Wassermann negative. Iodine uptake 10 per cent. Agglutinations, tests for *S typhosus.* H and O antigens, *brucella abortus, brucella proteus* (typhus) and paratyphoid A and B were all negative, occasional white blood cell and an occasional epithelial cell on microscopic examination. The basal metablosim on one occasion was plus 34 and when repeated it was plus 7.

X-ray studies:—Chest-cardiac silhouette normal. Lungs clear. Gallbladder negative for opaque or nonopaque calculi. Gastrointestinal series, including small intestines study, esophagus, stomach, and duodenum, were negative. There was an atypical entry of the terminal ileum into the cecum and ascending colon as mentioned, with an area of narrowing at the junction of the descending and sigmoid colons.

Gynecological consultations revealed a cystic enlarged cervix with incomplete stenosis. The fundus was three times the normal size, with irregular tumor masses. The adnexae were normal. On 26 March 1953, a laparotomy was performed.

May we see the films?

(Slide) Well, I would prefer to see the entire film. The rectum is large. Was there a scout film of the abdomen? There is some suggestion of a defect in the sigmoid colon. Let me see the next film.

Answer:—No we have no scout film.

Dr. Wangensteen:—There is no mention of great abdominal distention—there was some colic, and there is an irregularity in the sigmoid colon. Let us have a look at the x-ray films. May I see those? There is always an advantage, I feel, in seeing the film rather than a lantern slide reproduction.

(Film) I believe I can see the pattern of the colic mucosa at the site of the defect in the bowel.

(Film) Visualization of the mucosa at the defect would suggest an extramucosal lesion which, of course, would fit well with an endometriosis of the colon. Moreover, we are informed that the uterus is large.

Could it have been an ovarian cyst? Possibly so, but what of the bleeding into the peritoneal cavity and the blood in the stool? Could the lesion prove to be a malignancy, a cancer for instance? No, I do not think so; I remember the patient has had periodic bleeding for ten years. We do know that thyroid

tissue may occur in a dermoid ovarian cyst, but such cysts, apart from pressure phenomena, are often quite silent.

The responsibility of the surgeon is to diagnose the likely site of a lesion. He cannot always decide on its character. We are safe, I believe in diagnosing a lesion in the sigmoid colon; it looks to me like an extramucosal lesion, because one can see the pattern of the mucosa through it.

My diagnosis is partial obstruction of the colon with bleeding, owing probably to an extramucosal lesion—an endometrioma.

Let us hear what Dr. Snapper says.

Dr. Hertzog:—May I ask Dr. Snapper to comment?

Dr. Snapper:—You know what the law states, "Not twice for the same crime".

I think Dr. Wangensteen has an excellent point. The lesion may well be an endometrioma, transplanted during cesarean section,—an endometrioma of the intestine. I would have been more certain of this diagnosis if the lady had bled especially during menstruation.

Just to give the guessing game some flavor, I would like to mention another possibility. Sometimes polypoid lesions develop in a segmental colitis complicating a regional ileitis. The ileitis may be in the background, the colitis with watery diarrhea in the foreground. This would explain the diarrhea and the complaints of the upper abdomen. We don't have a complete small bowel series and what we see of it does not look like an enteritis.

I, therefore, agree with Dr. Wangensteen, that the lesion may well be an endometrioma. In order to avoid the impression of being a conformist I would like to suggest in addition that the possibility of a membraneous regional colitis which could have led to a stricture, is not excluded.

Dr. Hertzog:—We have a few minutes left. Would anyone on the floor like to ask any questions or make any diagnosis?

The surgeons who operated on this case were a little cagey. They thought she did have a uterine enlargement and that she should have a hysterectomy. They also said the colon should be investigated. The gynecologist removed the uterus, and the surgeons did a segmental resection of the colon. I will show you the gross specimen of the colon.

(Slide) We found a mass that involved the rectosigmoid, which was quite endurated. The serosa was puckered and deformed. The impression was that this was a carcinoma in this region.

(Slide) We opened up the specimen and, as Dr. Wangensteen predicted, it was an extramucosal lesion with intact mucosa over the lesion. Just why patient bled from this lesion is hard to say.

(Slide) Cutting through the wall of the bowel, the wall was found to be thickened, scarred and indurated. In this type of lesion, I think, it is difficult to be very definite about the gross finding. It could be a diverticulitis. We really have to depend upon the microscopic section.

(Slide) Microscopically it contained endometrial glands and endometrial stroma as seen in an endometrioma of the colon.

So, Dr. Wangensteen is right, this is an example of an endometrioma. The uterus removed showed multiple leiomyomas and also endometriosis of the Fallopian tubes. Endometriosis of the colon is not as rare as is reported in the literature. In the last five years we have had at Touro Infirmary, ten cases of endometriosis of the colon that came to surgery, and in the same time there were about 200 carcinomas of the colon, so our ratio is about 20 to 1.

I should like to ask Dr. Wangensteen to comment on his experience with endometriosis.

Dr. Wangensteen:—Uterine tissue can be transplanted. Victor Jacobsen of Albany many years ago ligated the Fallopian tubes in rabbits, causing the rabbits to menstruate into the peritoneal cavity. He got a large percentage of positive takes of endometrium in the peritoneal cavity of rabbits.

Dr. Joseph Meigs of Boston has been keen over advising young women in whom the diagnosis of endometriosis is made, to marry early and have children before the secondary effects of endometriosis set in. Some of the vagaries of endometrioma are very interesting, but it would take us far afield to discuss them.

Thank you Dr. Hertzog for having let me off so easily.

Dr. Snapper:—Dr. Hertzog, don't you think that the mucous membrane could have been completely different during the menstruation which then could explain the hemorrhages?

Dr. Hertzog:—That is probably the explanation as the overlying mucosa could become very congested and possibly ulcerate. The minute ulcers then heal promptly between periods.

Dr. Snapper:—Do you think it was a transplant after the cesarean section?

Dr. Hertzog:—Perhaps, but I prefer Robert Meyer's explanation that endometriosis represents a metaplasia of the celomic epithelium. The celomic epithelium is a very primitive tissue that has a great capacity to differentiate.

THE VALUE OF ROUTINE PROCTOSIGMOIDOSCOPY*

(A Continued Report)

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Just three years ago, in October of 1955, our group reported on the value of routine proctosigmoidoscopy. The study was based on 1,000 consecutive physical examinations on patients whose primary complaints were nonrectal. Polyps were found in 6.2 per cent of the thousand examinations, and 13 per cent of the polyps were malignant. Continuing the Sansum Medical Clinic study, this paper covers the incidence of positive findings from October of 1955 to March of 1958 in over 3,300 examinations.

Portes et al of Chicago surveyed 50,000 physical examinations, and published a well documented report on the same subject. Polyps were found in 7.9 per cent of the patients examined; malignant polyps occurred in 8.3 per cent of those patients with these lesions; and moderately advanced carcinoma was found in 0.035 per cent of the patients. The significance of these figures, and those of many cancer detection clinics, lies in the fact that almost all of the patients examined were asymptomatic.

A conference earlier this month by the New York State Society of Industrial Medicine was devoted to the value of routine proctoscopic examinations of employees in industry.

It is gratifying to all conscientious examining physicians to observe and study the increasing amount of attention being paid in the literature to this simple, but most important office procedure. It is still surprising, however, in spite of the volume of literature on the incidence of cancer of the colon and rectum in patients over 40, to discover what a small percentage of patients have ever had a proctosigmoidoscopic examination. It is likewise surprising that every physician does not routinely include this procedure in all complete physical examinations.

The premalignant potential of all polyps should be recognized. Cancer of the colon is the third most frequent malignant tumor found in both men and women. Benign mucosal polyps occur more frequently in males than in females, and can usually be located with the digital examination. But thorough proctosigmoidoscopic examination should certainly be achieved to discover any nonpalpable lesions.

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*Read before the Mexico Regional Meeting of the American College of Gastroenterology, Mexico, D.F., 27 October 1959.

From The Sansum Medical Clinic, Santa Barbara, Calif.

It is interesting to note that, in the present follow-up of our previously reported study, 7.7 per cent of the patients examined had polyps as compared to 6.2 per cent of the patients in our 1955 study. Of interest, also, is the fact that there were 44 cases, or 1.3 per cent, who had other lesions, such as ulcerative colitis or similar pathology.

Adenomas made up 45 per cent of the pathologic reports. Adenomatous or benign polyps made up 81 per cent of the total, with 18 per cent adenocarcinoma. The balance showed atypia.

Of the 302 patients with positive findings there were 198 males and 104 females. Cancerous polyps were found in 0.45 per cent of the males examined, and in 0.24 per cent of the females examined. This figure represents 65 per cent of all the adenocarcinomas found in males, and 35 per cent of adenocarcinomas found in females, in our series.

Adenomatous or benign polyps showed percentages of 61 per cent males and 39 per cent females. The average age was: male—54.3 years, ranging from 24 to 77; and female—53 years, ranging from 17 to 79.

Thorough preparation of the patient, both mechanically and from the psychological standpoint, is considered of the utmost importance. We have found the Fleet Enema Disposable Unit to be very satisfactory in the preparation of our patients for proctosigmoidoscopic examinations. As the examination itself progresses, the patient is kept aware of any significant findings, or the normalcy of appearance of the mucosa. This achieves relaxation on the part of the patient, as apprehension concerning what may be coming next is steadily dispelled through such reassurance.

Thoroughness, combined with gentle and tactful handling of the patient, can make the examination one that the patient will tolerate again in the future, as we feel that such examinations should be done, if not yearly, then at least on a biennial basis. This requires the cooperation of the patient.

The importance of the digital examination, and great care never to pass the proctoscope beyond this level until the light is in place, and the passage made under direct visualization, cannot be too strongly stressed.

Comment

More and more, with the widespread publicity made possible by modern methods of communication such as newspapers, magazines, radio and television, patients are being made aware of the importance of the proctosigmoidoscopic examination as a vital part of their general physical examination, particularly past the age of 40, and we feel that our figures substantiate the importance of this examination.

Summary and Conclusions

Very large series of routine proctosigmoidoscopic examinations have shown a percentage of positive findings comparable to those found in our Clinic in relatively asymptomatic patients in apparently normal health.

Polyps were found in 7.7 per cent of 3,321 routine proctosigmoidoscopic examinations. Malignant polyps were found in .69 per cent of the patients examined. The lack of clinical symptoms leading to the suspicion of polypoid lesions in the colon makes routine proctosigmoidoscopy the best method of detection of such lesions.

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EVALUATION OF AN ANTACID-ANTISECRETORY DRUG*

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Approximately $80,000,000 are spent each year in this country for the purchase of antacids, anticholinergic agents, and proprietary preparations for the relief of gastric distress[1]. Before prescribing any such medication it is important to know its pharmacologic and therapeutic effectiveness. Although innumerable studies have failed to reveal the exact cause of peptic ulceration, the predominant role of the proteolytic action of gastric hydrochloric acid and pepsin has been repeatedly demonstrated[2]. As a result drugs have been developed either to inhibit the secretion of, or to neutralize these factors. Recently a sustained action anticholinergic-antacid tablet (BepHan spacetab†) has become commercially available. This medication incorporates in one tablet the antisecretory-antispasmodic action of bellafoline (the levorotary alkaloids of belladonna) in a prolonged release form, and the acid neutralizing action of aluminum hydroxide-glycine and magnesium oxide. The present study was undertaken to evaluate this drug from chemical, pharmacologic, and therapeutic viewpoints.

Methods

Chemical evaluation of the antacid:—1. The volume of N/10 HCl neutralized by one BepHan Spacetab was determined by a slight modification of the procedure recommended in the Pharmacopeia of the U.S.A., XV[3]. One tablet was added to 100 ml. N/10 HCl in a 250 ml. flask. The flask was stoppered and placed in a 37°C. water bath for 1 hour with frequent shaking. An aliquot was then withdrawn and the excess acid titrated to a pH of 3.5 (Topfer's reagent) with N/10 NaOH. Because of the importance of antacid particle size in acid neutralization, the test was performed twice, once with a whole tablet and once with a pulverized tablet.

2. An *in vitro* imitation of neutralization in the continuously secreting and emptying stomach was performed using a modification of the method of Johnson and Duncan[4]. The study was performed as in 1. except that 2 tablets were used and 20 ml. of the reaction mixture were withdrawn as a representation of the physiological loss from the stomach, and 20 ml. of fresh N/10 HCl added to the system, as a representation of further gastric secretion, at 10-minute intervals,

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From the Department of Medicine, Orange County General Hospital, Orange, Calif.
†Trademark of Sandoz Pharmaceuticals.

for 90 minutes. The amount of "free acid" remaining at each time interval was determined by titration of the aliquot withdrawn with N/10 NaOH using Topfer's reagent. Studies were performed with both whole and pulverized tablets.

For the purpose of comparison, several commonly used antacid tablets were also evaluated in both phases of the chemical testing.

Pharmacologic evaluation:—The antacid and antisecretory effects of the drug were studied *in vivo* by means of gastric analyses and urinary uropepsin excretion rate determinations.

1. Gastric analysis:—Two-hour fractional gastric analyses were performed using either an Ewald Test meal or histamine as the stimulus. Two studies were performed on each patient, a control analysis in which no drug was adminis-

TABLE I

RESULTS OF GASTRIC ANALYSIS STUDY

Time of Administration of the BepHan Tablet	Decrease in Free Acid Concentration		
	None	Moderate	Marked
Before stimulus (½ hour)	5	1	
After stimulus	1	1	
Pulverized and suspended in tea of test meal	1		3

tered, and an analysis in which a BepHan Spacetab was administered. The order of performance of the two analyses was randomly varied from patient to patient. The form and time of drug administration also was varied, the tablet being given either one-half hour before ingestion of the test meal, testing antisecretory as well as antacid effect, or immediately after the stimulus, testing primarily antacid effect, and finally pulverizing the tablet and suspending it in the tea of the Ewald test meal.

2. Urinary uropepsin excretion rate:—The excretion rate of uropepsin was determined by the milk coagulation technic of West et al[5] with one important modification. Urine dilution studies revealed that the individual regression lines (uropepsin content on enzyme reaction time) for different urine specimens were only very roughly parallel, and hence the use of a common regression coefficient or slope as recommended by West et al, would introduce a large error. Therefore, a regression of uropepsin content on reaction time was obtained for each individual specimen by testing at least three dilutions (or urine volumes), fall-

ing within the range of the method, of each urine specimen. The amount of urine required to give the end point in 100 seconds (v') was then estimated graphically and the number of units excreted per hour calculated from the formula: Units/hr. = (Urine Volume)/v' x hours of collection x 10). The four-hour fasting morning urine specimen was used[5]. At least two studies were per-

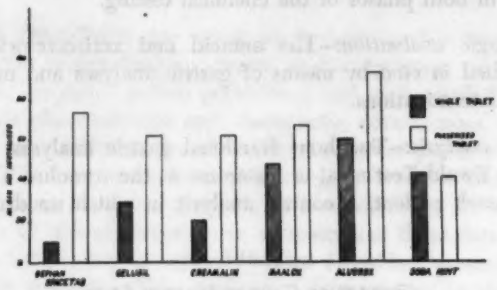

Fig. 1—Acid neutralization by different antacid tablets, whole and pulverized.

formed with each patient, a control test, and a drug test in which one BepHan tablet was ingested at bedtime and one at the start of the urine collection period.

Therapeutic evaluation:—Patients seen in the gastrointestinal clinic and medical ward complaining of epigastric distress for which antacid or anticholinergic therapy was indicated, e.g. duodenal ulcer, hiatal hernia, psycho-

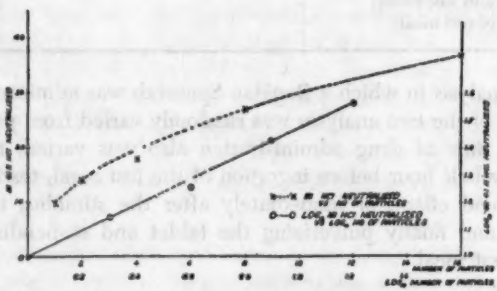

Fig. 2—Relationship between volume of acid neutralized and number of antacid particles, the total amount of antacid being constant.

physiologic gastrointestinal reaction, were placed on BepHan therapy plus an appropriate diet. The time of ingestion of the tablet was varied, initially one tablet two or three times daily being prescribed, later one tablet before meals and at bedtime, and lastly one tablet one hour after meals and at bedtime. The patients were instructed to chew the tablet thoroughly.

Results

Chemical evaluation of the antacid:—In Figure 1 the volume of N/10 HCl neutralized by 1 tablet, whole and pulverized, of the different antacids tested, is presented graphically. These results are the average of two or three individual determinations, and in each instance the replicate determinations yielded similar results. The whole BepHan tablet did not disintegrate well, and, as can be seen, yielded poor neutralization. When pulverized, however, considerable improvement was obtained in acid neutralization. Of the antacid tablets tested, only the Aludrox tablet exceeded the pulverized BepHan tablet in neutralizing capacity. It is of considerable interest that the Aludrox, soda mint, and Maalox tablets disintegrated moderately easily and yielded fairly good results even when not pulverized.

TABLE II

Results of Uropepsin Excretion Rate Study

	Number of Studies in which Uropepsin Excretions:		P Level for the Sign Test
	Increased	Decreased	
Total studies	10	15	> 25%
Patients secreting < 15 U/hr.	8	2	25%
Patients secreting > 15 U/hr.	2	13	1%

The importance of the degree of disintegration or number of particles available for reaction with the acid is further demonstrated in Figure 2. BepHan Spacetabs were divided into halves, quarters, eighths and sixteenths, and the amount of N/10 HCl neutralized by one tablet in each of these forms determined as above. Results of a typical study are presented in Figure 2. The relationship between the number of particles and acid neutralization is a logarithmic one and not a simple linear one. As the number of particles available for neutralization increases there is a disproportionate increase in volume of acid neutralized. Upon log-log graphing, this relationship becomes linear, indicating the volume of acid neutralized is related to the number of particles available raised to the power of the slope of the line.

The results of the *in vitro* imitation of neutralization in the continuously secreting and emptying stomach using two whole tablets and two pulverized tablets are graphically presented in Figures 3 and 4 respectively. The BepHan

tablet disintegrated poorly and exhibited only minimal antacid effect when not pulverized (Fig. 3). In contrast, the Maalox and Aludrox tablets disintegrated more readily and neutralized large amounts of acid even when not pulverized, the Aludrox tablet exhibiting greater antacid effectiveness. When pulverized (Fig. 4), all tablets tested revealed considerable antacid effect. The Aludrox tablet again proved to be the most efficient antacid of the tablets tested. BepHan, while taking longer to reach maximum neutralization and not reaching the peak antacid activity of the Maalox tablet, had a more sustained effect than either the Maalox or Gelusil tablets.

Pharmacologic evaluation:—I. Results of gastric analysis study:—The results of a total of 12 gastric analysis studies are presented in Table I. Moderate effect indicates depression by BepHan of free acid concentration to one-third or less of that in the comparable period in the control study for one-half hour or more. Marked effect indicates depression by BepHan of free acid concentration to below the control study levels throughout the entire period of the study and to

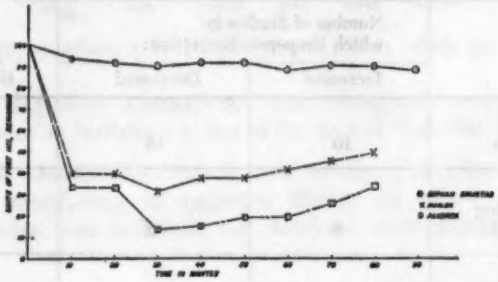

Fig. 3—*In vitro* imitation of gastric acid neutralization by different antacid tablets, whole.

one-fourth or less of the comparable control period levels for one hour or more. The Ewald Test meal was used as the stimulus in all studies except three of the "Before Stimulus" studies, in which instances histamine was used, and in one of these a moderate drug effect was obtained. It is to be noted that only when the tablet was pulverized and suspended in the tea of the test meal was a marked effect obtained. In two of these studies no free acid was present for over one hour during the drug study. A graph of the mean values of the four studies in this group is presented in Figure 5. Considerable free acid depression was noted during the second hour as well as during the first hour of the study. This could be due to an antisecretory effect and/or antacid effect plus decreased gastric emptying and motility. The failure to obtain a decrease in free acid in five of the six studies in which the drug was administered before the meal is evidence against a significant antisecretory effect.

2. *Results of urinary uropepsin excretion rate tests:*—The results of a total of 25 studies are presented in Table II. In 10 of the tests the control uropepsin

excretion rate was below the lower limits of normal (15 uropepsin units per hour) and hence this group was separated, for purposes of analysis, from the normal and hypersecretors (15 to 40, and over 40 uropepsin units per hour respectively) in which categories duodenal ulcer patients characteristically fall. These studies were performed on patients selected at random from a general medical ward having many elderly patients and were not restricted to patients with gastrointestinal disorders. This accounts for the large number of hypo-

TABLE III

RESULTS OF THERAPEUTIC EVALUATION

	Time of BepHan Administration	Diagnosis	Total Cases	Results		
				Good	Fair	Poor
I	Two times daily, three times daily, or before meals and at bedtime.	Psychophysiologic gastrointestinal reaction	8	2		6
		Duodenal ulcer	8	3		5
		Hiatal hernia	2			2
		Subtotal	18	5		13
II	One hour after meals and at bedtime.	Psychophysiologic gastrointestinal reaction	8	3	2	3
		Duodenal ulcer	10	7		3
		Gastric ulcer	1		1	
		Hiatal hernia	3	1	1	1
		Postbulbar ulcer	2	2		
		Duodenitis	3	2	1	
		Subtotal	27	15	5	7
		Total	45	20	5	20

secretors tested. The simple sign test* was applied to these two groups and to the group as a whole (third column, Table II). No significant effect of BepHan was found in the hyposecretors. With, however, those patients excreting over 15 units per hour, depression of uropepsin excretion occurred in 13 out of 15 studies. There is only 1 chance in 100 of obtaining such results if there were no significant effect of BepHan. It is concluded therefore, at the 1 per cent

*The sign test is not ordinarily used on samples of small size except for preliminary or rough work[6]. The results of this analysis are included here solely to indicate that these limited studies do point towards a significant effect of BepHan on uropepsin excretion.

level of significance, that the BepHan Spacetab produced depression of uropepsin excretion. The average control uropepsin excretion rate in these 15 patients was 43 units per hour, and the average depression following BepHan administration was 19 units.

Therapeutic evaluation:—A total of 45 patients received BepHan Spacetabs for the relief of epigastric distress. The clinical diagnoses are listed in Table III. Only the response of the acute attack to the medication was evaluated in this

TABLE IV

CHI-SQUARE TEST. THERAPEUTIC EFFECTIVENESS OF BEPHAN SPACETABS CLASSIFIED ACCORDING TO TIME OF ADMINISTRATION OF THE MEDICATION

Therapeutic Regimen		Results			Total
		Good	Fair	Poor	
I	f	5	0	13	18
	F	8	2	8	
	$f - F$	−3	−2	5	
II	f	15	5	7	27
	F	12	3	12	
	$f - F$	3	2	−5	
Total		20	5	20	45

$$X^2 = \Sigma \frac{(f - F)^2}{F} = 10.417,\ d.f. = 2$$

I = BepHan Spacetabs administered two times daily, three times daily, or before meals and at bedtime.
II = BepHan Spacetabs administered one hour after meals and at bedtime.
f = observed frequency.
F = hypothetical frequency.
$d.f.$ = degrees of freedom.

study. No long term follow-ups are available concerning the effectiveness of prolonged BepHan medication on chronic problems such as duodenal ulcer recurrence. The over all results (Table III) reveal only 20 patients obtained good relief of symptoms, and 5 fair relief, while 20 obtained poor relief. Analysis of results according to time of BepHan administration, however, uncovers important information. In the early phase of the study, BepHan was prescribed twice daily in accordance with the manufacturer's recommendations. The failure of this regimen to afford relief of symptoms resulted in our increasing the fre-

quency of drug administration to three times daily, later to four times daily, before meals and at bedtime, as antisecretory drugs are commonly prescribed, and finally to four times daily, one hour after meals and at bedtime, as antacids are commonly prescribed. As can be seen in Table III, only with administration of BepHan after meals and at bedtime were favorable therapeutic results obtained. Of the 27 patients in this group, only 7 failed to obtain some degree of relief of symptoms, while 15 obtained good relief, and 5 fair relief.

Inasmuch as all patients were placed on the same treatment regimen except for the time of administration of BepHan, the first group of patients form a control study for the statistical evaluation of the after meal-bedtime regimen group. A 2 x 3 contingency table was drawn and the chi-square test performed[7] as shown in Table IV. The resulting chi-square value, 10.417, with two degrees of freedom, is significant at the 1 per cent probability level, indicating that the better therapeutic results with the after meal-bedtime administration of BepHan is very probably due to more than chance*.

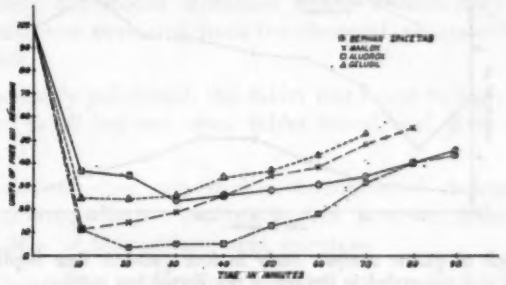

Fig. 4—*In vitro* imitation of gastric acid neutralization by different antacid tablets, pulverized.

Ten patients complained of side-effects of the medication and only three of these patients obtained relief of symptoms. Three of these patients complained of nausea, two of a "bad taste" in their mouths, three of a dry mouth, one of blurred vision, two of frontal headache and two of constipation. In addition three patients noted adherence of the BepHan particles to their dentures, making cleaning of the dentures difficult.

Comment

In the tablet form of antacid therapy, degree of disintegration (and hence surface area available for interaction) of the tablet is extremely important. This was clearly demonstrated in the present study by: 1. the improvement in *in vitro* acid neutralization by nearly all tablets tested when pulverized, 2. the

*Because allocation of patients to each treatment group was not randomized, all patients having been placed on one treatment regimen at one time, and all new patients on another at a later date, the possibility of this factor introducing a bias remains.

logarithmic relationship between the volume of acid neutralized and the number of antacid particles, the total amount of antacid being constant, and 3. improvement in *in vivo* acid neutralization (gastric analysis study) when the tablet was prepulverized. When properly pulverized, the BepHan Spacetab demonstrated good antacid effect both *in vitro* and *in vivo*. In a recent clinical report Weiss et al[8] found that a more favorable therapeutic effect was obtained when the BepHan Spacetab was chewed before swallowing than when the tablet was ingested whole. These findings indicate the importance of further attempts to develop a nonabsorbable antacid tablet that disintegrates readily.

The antisecretory effect of the BepHan Spacetab was not as clearly shown. The gastric analysis study failed to demonstrate an unequivocal antisecretory effect. These tests, however, evaluated only the effect on concentration of acid

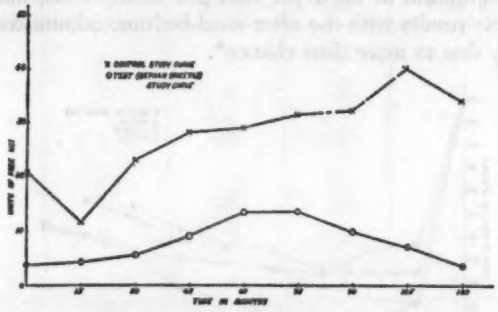

Fig. 5—Mean graph of gastric analysis study in four patients. One BepHan Spacetab was pulverized and suspended in the tea of the Ewald test meal.

in the stomach and did not evaluate any possible effect on volume of acid secreted. Antisecretory efficacy was also studied, albeit indirectly, by noting the variation in uropepsin excretion following drug administration. Hollander and Janowitz[9] have shown that the amount of uropepsin appearing in the urine is proportional to the amount of pepsin secreted into the stomach. BepHan administration did result in a significant decrease in the uropepsin excretion rate in normal and hypersecretors, indicating an antisecretory effect of the drug.

The importance of time of administration of the BepHan Spacetab was revealed in the clinical phase of the study. Poor therapeutic results were obtained in a majority of the patients when the drug was administered two or three times daily, or before meals and at bedtime. Good results were obtained in a majority of the patients, a statistically significant improvement, when the drug was administered one hour after meals and at bedtime. This could be interpreted as indicating 1. primarily an antacid effect of the medication, or 2. an antacid effect plus a decrease in gastric emptying due to an inhibition of gastric motility, or 3. an antacid effect plus a carryover of the antisecretory

effect of the previously administered long-acting tablet. Relief of symptomatology could also be due to relief of gastrointestinal spasm due to the antivagal action of the drug. Although the effect on gastrointestinal motility was not evaluated in this study, studies by others[10] have shown a significant antispasmodic effect by bellafoline, the antivagal ingredient in the BepHan Spacetab.

From a practical point of view, tablet medication is advantageous for those individuals who find it inconvenient to carry a bottle of liquid medicine. The combination of an antacid and an antisecretory drug in a long-acting form in one tablet eliminates the taking of two separate medications. The recently introduced sustained action antacid-antisecretory tablet, BepHan Spacetab, has been shown in this study to be therapeutically effective when chewed thoroughly and administered one hour after meals and at bedtime, and warrants further clinical evaluation on a wider scale.

Summary

1. A recently introduced sustained action antisecretory-antacid tablet, BepHan Spacetab, was evaluated from the chemical, pharmacologic and therapeutic viewpoints.

2. When properly pulverized, this tablet was found to have *in vitro* antacid efficacy superior to all but one other tablet tested, and good *in vivo* antacid effect.

3. Uropepsin excretion rate studies demonstrated depression of pepsin secretion by this drug. Gastric analysis studies, however, failed to reveal unequivocal inhibition of hydrochloric acid secretion.

4. Good therapeutic results were obtained in a majority of patients complaining of epigastric distress when one tablet, thoroughly chewed, was taken one hour after meals and at bedtime.

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MAINTENANCE THERAPY IN GASTROINTESTINAL DISORDERS

18-Month Study of a New Anticholinergic

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Cincinnati, Ohio

Results of antisecretory and antispasmodic tests following the administration of isopropamides*, a new long-acting anticholinergic, indicate that this drug reduces gastric acidity and gastrointestinal motility for periods of at least 12 hours after a single dose[1,2,3]. Clinical results following the short-term, twice-a-day use of this drug have been reported by the author[4] and others[5,6], and indicate that it satisfactorily controls the symptomatology of common organic and functional gastrointestinal disorders. Only one report[7] has appeared describing the continuous, long-term (up to one year) use of isopropamide in treating gastrointestinal disease (peptic ulcer). Because the value of maintenance or prophylactic therapy in gastrointestinal diseases has not, as yet, been clearly defined, the evaluation reported herein was undertaken with isopropamide to obtain additional information on the effects of anticholinergic maintenance therapy on the chronicity of common gastrointestinal disorders.

Method and Material

Seventy-four patients with a variety of common gastrointestinal disorders (see table) were selected for the evaluation. The duration of digestive disorders varied greatly (6 months to 15 years); medical histories revealed a fairly well-established pattern of symptom recurrences, particularly for patients with peptic ulcer. Results following the short-term (average 5.1 months) use of the drug have been reported elsewhere[4]. Briefly, 62 (84 per cent) of the patients obtained complete relief of symptoms; 10 (14 per cent) obtained partial relief; and 2 (2 per cent) failed to derive any benefit from the drug. Sixty-four of these patients have remained under medical supervision for periods ranging from 6 to 18 months (average 16.3 months), and form the basis of this report.

When first seen, all patients had one or more symptoms of active gastrointestinal disease and underwent gastric analyses, urinalyses, radiographic examinations, and complete blood tests. In addition to rigidly controlled diets and multiple feedings, patients received doses of isopropamide varying from 5 mg. q12h to 10 mg. q12h. Once symptoms were controlled, patients were continued on maintenance doses of either isopropamide or a combined preparation of isopropamide and prochlorperazine†, the latter in sustained release form. Maintenance doses of 5 mg. of isopropamide were taken once (usually in the morn-

*Supplied as "Darbid", Smith, Kline & French Laboratories, Philadelphia, Pa.

†Supplied as Combid Spansule Capsules, Smith, Kline & French Laboratories, Philadelphia, Pa.

ing) or twice a day. Maintenance doses of the combined preparation were essentially the same; each sustained release capsule of the preparation contained 5 mg. of isopropamide and 10 mg. of prochlorperazine. During this period, diets were progressively modified in size, frequency, and diversity until they approached normal. After normal eating patterns had been established and the patient had remained symptom-free for approximately 3 months, medication was gradually withdrawn from the regimen. Withdrawal of the medication generally required two or three months. If symptoms recurred during this period, one of the medications was restored to the regimen, and the diet was modified. When symptoms were controlled, the usual method was used to withdraw medication.

TABLE I

RESULTS OF MAINTENANCE THERAPY WITH ISOPROPAMIDE AND ISOPROPAMIDE AND PROCHLORPERAZINE

Diagnosis	No. Pts. Treated	No. Pts. Followed	Av. Follow-up Period (mos.)	No. Pts. Off Drugs	No. Pts. On Drugs	Results		
						Good	Fair	Poor
Duodenal ulcer	36	32	17.4	24	8	26	5	1
Gastric ulcer	10	8	16.7	5	3	8	—	—
Gastroduodenal	9	8	17.6	7	1	7	1	—
Gastritis (chronic)	9	8	16.0	6	2	7	1	—
Pancreatitis	6	5	16.1	3	2	3	1	1
Esophageal hiatus hernia	4	3	14.0	2	1	1	2	—
Total	74	64	16.3 (Av.)	47	17	52	10	2

Patients were requested to undergo repeat laboratory examinations after they had been asymptomatic for six months, or sooner if symptoms recurred. As might be expected, not all patients submitted to a second laboratory examination. Those that did not were given complete physical examinations and were interviewed (as were all patients) regarding their state of health during the interim when they were not receiving medication.

RESULTS

Results were classified as: "Good"—no recurrence of previously elicited symptoms; "Fair—recurrence of previously elicited symptoms requiring reinstitution of medication and dietary modification: "Poor"—recurrence of previously elicited symptoms with complications (hemorrhages or perforations) that required surgery. Whenever possible, results of laboratory re-examinations were used as an aid in classifying results.

At the conclusion of the evaluation, 47 (73 per cent) of the patients were no longer on medication. The duration of therapy for these patients averaged 7.4 months; the majority of these patients had not received medication for 8 months or longer at the time of their final visit. The remaining 17 (27 per cent) patients still required medication, usually once a day. In this group, the duration of therapy averaged 16.5 months. All but two of these patients were receiving the combined isopropamide-prochlorperazine preparation. The addition of prochlorperazine, a tranquilizing agent related to chlorpromazine, to isopropamide seemed warranted in these patients because their gastrointestinal symptomatology appeared related to unresolved anxiety-producing personal situations.

Results of therapy during the maintenance and follow-up periods are given in the table. As will be noted, 52 (81.2 per cent) of the patients obtained good results; 10 (15.6 per cent) obtained fair results; and 2 (3.2 per cent) obtained poor results. These results compare favorably with those obtained during the short-term use of the drug. Of the patients who obtained fair results, the recurrence of their symptoms was decreased in incidence and severity. Three of these patients had not received medication for periods of from two to three months prior to the recurrence of symptoms. Both patients who required surgery had been off medication only a short time (less than a month) when their symptoms returned.

Although over 80 per cent of the patients did not experience a recurrence of symptoms while receiving therapeutic and maintenance doses of isopropamide or the isopropamide-prochlorperazine preparation, the exact role these drugs played in affecting the established pattern of recurrences is difficult to evaluate. The concomitant use of rigidly controlled diets and the tendency for gastrointestinal lesions to heal spontaneously cannot be discounted as factors which may have influenced these results. The addition of the tranquilizing agent in the form of the combined isopropamide-prochlorperazine preparation, however, proved useful in the 15 patients who "required" continual medication because of unresolved anxiety-producing personal conflicts. More than three-fourths of these patients had experienced remission of symptoms while receiving adequate therapy with anticholinergic drugs alone, but the remissions were always short-lived. It would appear that the control of emotional factors by the prochlorperazine component of this preparation was responsible for the prolonged (up to a year in some patients) freedom from the recurrence of gastrointestinal symptoms in these patients.

Results of repeat laboratory examinations in 16 patients were unremarkable. Gastric or duodenal lesions previously demonstrated were healed or virtually healed in most patients and, although not unusual, results of gastric analyses in patients with duodenal ulcers who had been off medication were little different from the values obtained in previous tests that had been completed before the

patients were placed on therapy. Complete blood counts did not reveal any abnormal hematologic changes.

Since all the patients had previously received anticholinergic drugs for prolonged periods in most cases, the usual side-effects with these drugs were expected and tolerated. As reported in the previous study, side-effects with isopropamide were mild and transient and did not preclude the use of the drug in any of the patients. No side-effects were encountered by any of the patients receiving the combined isopropamide-prochlorperazine preparation. Although the drugs were used for as long as 16 months in some cases, none of the patients reported a tolerance to therapeutic effects of these drugs.

Comment

The over all results of therapeutic and maintenance therapy obtained in this evaluation, although slightly less impressive, compare favorably with those reported by Cayer[7]. It should be pointed out, however, that the incidence of recurrences (18.7 per cent) reported herein is less than one-third that (64.0 per cent) reported by the latter investigator for patients with peptic ulcer. It is interesting to speculate about the reasons that may have accounted for this. Because half the patients in this evaluation were treated for gastrointestinal disorders in which recurrences rarely follow an established pattern, one could speculate that this may have accounted for the difference. An inspection of the incidence of recurrences (15.6 per cent) for only those patients with peptic ulcer, however, does not bear out this assumption. That a difference of this magnitude could have resulted from patient individuality or their attitudes regarding faithfulness to prolonged therapy after they had become asymptomatic is unlikely since you would expect, unless the group of patients did not represent a true "cross-section", these individual differences to cancel each other. The inability to explain this difference seems to point up the difficulty in trying to evaluate maintenance therapy in disorders of this type, and is further evidence that we know relatively little about the multiplicity of factors involved in the production of gastrointestinal disorders and the "perpetuation" of symptom recurrences.

While the maintenance use of isopropamide and of the combined isopropamide-prochlorperazine preparation apparently eliminated, at least for the duration of this evaluation, the recurrences of gastrointestinal symptoms in a large percentage of the patients treated, it is rather obvious that it did not prevent the recurrence of symptoms or conditions (hemorrhages or perforations) in all patients. The results do indicate, however, when compared to results reported for patients receiving placebo medication[8], that patients have fewer and possibly milder recurrences of symptoms when they are maintained on adequate therapy with potent drugs such as the ones used in this evaluation and when they avail themselves of frequent medical examinations and counseling.

Summary

The long-term use of a new, long-acting anticholinergic, isopropamide, and of a combined preparation of this drug and prochlorperazine in patients with common gastrointestinal disorders is described. Results indicate that the incidence of symptom-recurrences were eliminated in over 80 per cent of the patients, and were decreased and made milder in 16 per cent of the patients. Four per cent of the patients did not benefit from these medications and required surgery. The results of therapy are discussed and compared with those of other investigators.

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President's Message

This being my last opportunity as President to contact the members of the American College of Gastroenterology, I want to take this occasion to thank the Officers, Board of Trustees and Governors as well as the entire membership for their support during my administration. It was no easy matter to follow in the footsteps of Dr. C. Wilmer Wirts, the Past-President; and I sincerely wish continued success in making our organization outstandingly prominent to Dr. Joseph Shaiken, the President-Elect. If I have been stern or occasionally harsh, I believe I have been fair in my decisions, and have always acted accordingly with the best interests of the College in mind. I want to thank all the members of the various committees and especially those Chairmen who have done such excellent work making the coming convention so complete. Dr. Donald C. Collins and Dr. George K. Wharton have been unusually helpful and cooperative in this regard.

My "sympathies" go to the Executive Director for the many problems which present themselves in preparing for the postgraduate and scientific programs, postconvention meetings, regional meetings, publication of the Journal, etc. Therefore, I want to take this opportunity to thank Daniel Weiss for his many efforts in helping me meet printing deadlines, arrange committee meetings, plan for future conventions and generally make the presidential office so much easier. Without his cooperation I am sure I could not have successfully carried on during this administration in view of the heavy teaching load at the Medical School, in addition to all the many extracurricular activities put upon me. My thanks and wishes for future success go to him.

Awaiting anxiously our meeting with you in Los Angeles and Honolulu in September, I remain

Frank J. Borrelli

NEWS NOTES

Twenty-Fourth Annual Convention

When the American College of Gastroenterology meets at the Biltmore Hotel in Los Angeles, Calif. this month, it will be our first meeting on the West Coast since 1953.

Following the usual pattern, the business sessions will commence with committee meetings on Saturday, 19 September 1959, to be followed on Sunday, 20 September 1959, with the Annual Meeting of the Board of Trustees, a luncheon for the Board of Trustees and the Board of Governors and the Annual Meetings of the Fellowship of the College and the Women's Auxiliary.

The Fellows will vote for Officers, Trustees and Governors and on the adoption of amendments to the Constitution and By-laws.

In addition to their business meeting, the Women's Auxiliary will have a luncheon at the Biltmore Hotel starting at 1:00 P.M., on Sunday, 20 September 1959.

At our Annual Convocation Ceremony in the Renaissance Room on Sunday at 6:30 P.M., certificates will be presented to Honorary Fellows, newly elected and advanced Fellows and Associate Fellows.

The principal speaker will be Dr. Stafford L. Warren, Honorary Fellow of the College, who is Dean of the School of Medicine at the University of California at Los Angeles. Dr. Warren will speak on "Medicine in the Atomic Age".

Following the Convocation Ceremony, at 8:30 P.M., we will again enjoy a buffet supper sponsored by William H. Rorer, Inc., of Philadelphia, Pa. Tickets of admission will be given out at the Convocation Ceremony. An excellent motion picture, "Wild Flowers of the West", in color, will be shown through the courtesy of the Richfield Oil Corp.

The scientific sessions will be held in the Ballroom on Monday, Tuesday and Wednesday, 21, 22, 23 September and will feature individual papers on topics of current interest in the fields of gastroenterology and allied subjects.

The technical and scientific exhibits, carefully selected, will be located on the Galeria and in the Ballroom Foyer. The registration desk will be immediately outside of the entrance to the Foyer.

The House of Seagram will once again serve coffee and sweet rolls in the exhibit area each morning from 8:30 to 9:30.

At noon on Monday, out hosts for luncheon will again be Burton, Parsons & Co. of Washington, D.C. Tickets for the luncheon will be available at the registration desk.

On Monday evening from 6:30 to 8:30, the Smith-Dorsey Division of The Wander Company will sponsor the President's Reception and cocktail party, at which Dr. Andrew Muir of Scotland will be the guest of honor. Cards of admittance to the reception will be available at the registration desk.

Tuesday at noon, the Board of Governors will have their Annual Luncheon Meeting in Conference Room 4.

That evening, we will have our Annual Dinner-Dance in the Renaissance Room. Tickets will again be sold by tables and those desiring to sit at the same table, are urged to purchase their tickets at the same time or have one of their number, purchase tickets for the entire group.

Twenty-five year certificates will be presented to 16 members of the College, signifying their continuous membership in the organization.

Our new President, Dr. Joseph Shaiken of Milwaukee, Wisc., will be inaugurated and will be given the insignia of office by Dr. Frank J. Borrelli of New York City, the retiring President.

There will be dancing to the music of Ivan Scott and his orchestra as well as other entertainment.

On Wednesday, the newly elected Board of Trustees will have its luncheon in Conference Room 4.

An outstanding scientific program and Postgraduate Course has been prepared by our Program Committee under the chairmanship of Dr. George K. Wharton. Dr. Donald C. Collins is the Over all Chairman, who has arranged the activities other than those of the scientific programs.

A copy of the program appears elsewhere in this issue and members of the College will receive theirs additionally in the mail. Copies are also available from the headquarters office, 33 West 60th Street, New York 23, N. Y.

Women's Auxiliary Program

An exciting and interesting program for the wives and families of the doctors attending the Convention has been prepared by Mrs. George K. Wharton, assisted by Mrs. Dale W. Creek, Mrs. Lester M. Morrison and the other ladies. The complete details are being sent out by mail.

Briefly, the program is as follows:

Sunday, 20 September 1959

Registration will open at 11:00 A.M., on the Galeria Floor of the Biltmore Hotel. Final arrangements and purchase of tickets for the various activities should be made at this time.

At 1:00 P.M., the ladies will have lunch at the Biltmore Hotel.

The business meeting of the auxiliary and election of officers will take place at 2:30 P.M.

The Convocation Ceremony of the College, to which the ladies are invited, will be held at 6:30 P.M., followed by the buffet supper and a motion picture.

Monday, 21 September 1959

The registration desk will be open at 8:30 A.M.

At 9:15 A.M., the bus will leave from the Biltmore Hotel for a sightseeing trip to St. Sophia Cathedral and then on to the Art Linkletter show. Lunch will be at the world famous Farmers Market and at 1:30 P.M., the bus will leave the Market for a tour of Universal City, the home of Universal-International Studios and the Taluca Lake homes of the movie stars.

In the evening, the ladies are invited to attend the President's Reception and Cocktail Party from 6:30 to 8:30 P.M.

Tuesday, 22 September 1959

The registration desk will be open at 8:30 A.M.

A bus tour to Beverly Hills, beaches and more homes of movie stars will leave the Biltmore Hotel at 9:00 A.M.

There will be a luncheon and fashion show at the Beverly-Hilton Hotel at 12:30 P.M. and then the afternoon will be free.

At 7:00 P.M., the Annual Dinner-Dance of the College, preceded by cocktails, will be held at the Biltmore Hotel. This will be informal with dancing and entertainment.

Wednesday, 23 September 1959

The morning has been left open for individual activities.

Buses will leave the Biltmore Hotel at 2:00 P.M. for an afternoon at Disneyland.

Reservations for all activities are required and should be made in advance.

Doctor's Registration

Registration for doctors will be open at 1:00 P.M., on Sunday, 20 September 1959, outside the Ballroom Foyer in the Biltmore Hotel.

The registration desk will be open until 5:00 P.M. on Sunday. On Monday, Tuesday and Wednesday, the registration desk will be open from 8:30 A.M. until 4:30 P.M.

An identification badge will be issued to those who register and no one will be admitted to the exhibits or the sessions without it.

Annual Meeting Board of Trustees

The Board of Trustees of the American College of Gastroenterology will hold its Annual Meeting at the Biltmore Hotel in Los Angeles, Calif., at 9:00 A.M. on Sunday, 20 September 1959. There will be a joint luncheon with the Board of Governors at 1:00 P.M.

Annual Meeting American College of Gastroenterology

The Annual Meeting of the Fellows and Life Fellows of the American College of Gastroenterology will take place at the Biltmore Hotel in Los Angeles, Calif., at 3:00 P.M., on Sunday afternoon, 20 September 1959. Election of officers, trustees and governors will be held.

Convocation Ceremony

There will be a rehearsal (without caps and gowns) for the Convocation Ceremony in the Renaissance Room at the Biltmore Hotel at 4:15 P.M., on Sunday, 20 September 1959.

Those participating are asked to obtain their caps and gowns and be ready for photographs by 6:00 P.M.

The convocation itself will take place in the Renaissance Room at 6:30 P.M., and Dr. Stafford L. Warren will be the speaker.

William H. Rorer, Inc. Buffet Supper

This year again, the buffet supper following the convocation, will be sponsored by William H. Rorer, Inc. It will be held at 8:30 P.M., in the Music Room. Only those attending the Convocation Ceremony will receive tickets of admission.

There will be a movie shown following the supper.

Scientific Exhibits

The Committee on Scientific Exhibits under the chairmanship of Dr. Lester M. Morrison, has selected a number of interesting and instructive scientific

exhibits. These will be on display on the Galeria from Monday morning, 21 September 1959 through noon on Thursday, 24 September 1959.

The committee will award certificates and ribbons for the best exhibits.

Burton, Parsons & Co. Luncheon

On Monday, 21 September 1959, Burton, Parsons & Co., will again sponsor a luncheon at 12:30 P.M. There will be a noted speaker whose name will be announced at that time.

Cards of admission may be obtained at the registration desk outside the Ballroom Foyer.

Credentials Committee

The Credentials Committee will meet at 5:00 P.M., on Monday, 21 September 1959 at the Biltmore Hotel in Los Angeles, Calif. Only those applications received by 7 September 1959 will be considered.

Smith-Dorsey Cocktail Party

The President's Reception and Cocktail Party, sponsored by the Smith-Dorsey Division of The Wander Company, in honor of Dr. Andrew Muir of Scotland, will be held from 6:30 to 8:30 P.M., on Monday, 21 September 1959.

Invitations will be available at the registration desk.

Annual Meeting Board of Governors

The Board of Governors of the American College of Gastroenterology will hold their Annual Meeting and Luncheon at the Biltmore Hotel in Los Angeles, Calif., at 12:30 P.M., on Tuesday, 22 September 1959.

The agenda includes the election of a chairman and the appointment of committees.

Annual Dinner-Dance

On Tuesday evening, 22 September 1959, the College will hold its Annual Dinner-Dance in the Renaissance Room of the Biltmore Hotel in Los Angeles, Calif.

Cocktails will be served starting at 7:00 P.M. and there will be dancing and entertainment.

Tickets will cost $10.00 per person and will be available in advance. Reservations for the dinner will close at 10:00 A.M., on Tuesday, 22 September 1959.

As tickets will be sold by table numbers only, those wishing to sit together are requested to purchase their tickets at the same time.

Board of Trustees Luncheon

A luncheon meeting of the newly elected Board of Trustees will be held at 12:30 P.M., on Wednesday, 23 September 1959. The election of a chairman and the appointment of committees will take place at this time.

Course in Postgraduate Gastroenterology

The Annual Course in Postgraduate Gastroenterology of the American College of Gastroenterology will be held at the Biltmore Hotel in Los Angeles, Calif., 24, 25, 26 September 1959. An afternoon session will be held at the College of Medical Evangelists.

The faculty for the Course will, for the most part, be from the staffs of the medical schools in Los Angeles.

Only those presenting matriculation cards, indicating that they have registered and paid the fee, will be admitted to the Course sessions.

Hawaii Regional Meeting

Following the adjournment of the sessions in Los Angeles on Saturday, 26 September 1959, the meeting will reconvene in Honolulu, Hawaii on Sunday, 27 September 1959 at 10:00 A.M. The program will consist of a panel discussion put on by doctors from our 50th state and individual papers and another panel by members of the American College of Gastroenterology.

Nominating Committee Report

The nominating Committee of the American College of Gastroenterology, consisting of Dr. C. Wilmer Wirts, Philadelphia, Pa., Chairman, Dr. Joseph Shaiken, Milwaukee, Wisc.; Dr. Stanley S. Sidenberg, Cleveland, Ohio; Dr. Joseph E. Walther, Indianapolis, Ind. and Dr. Stanley H. Craig, New York, N. Y., has submitted the following slate of candidates to be voted upon at the Annual Meeting of the Fellowship of the College in September.

Officers

President-Elect	Henry Baker, M.D., Boston, Mass.
1st Vice-President	Louis Ochs, Jr., M.D., New Orleans, La.
2nd Vice-President	Edward J. Krol, M.D., Chicago, Ill.
3rd Vice-President	Theodore S. Heineken, M.D., Glen Ridge, N. J.
4th Vice-President	Henry G. Rudner, Sr., M.D., Memphis, Tenn.
Secretary-General	Lynn A. Ferguson, M.D., Grand Rapids, Mich.
Secretary	Leonard Troast, M.D., Jersey City, N. J.
Treasurer	William C. Jacobson, M.D., New York, N. Y.

Board of Trustees

For 3 years:	Max Caplan, M.D., Meriden, Conn.
	Murrel H. Kaplan, M.D., New Orleans, La.
	Milton J. Matzner, M.D., Brooklyn, N. Y.
	Louis L. Perkel, M.D., Jersey City, N. J.
	Julian A. Sterling, M.D., Philadelphia, Pa.

Board of Governors

District of Columbia	Henry A. Monat, M.D., Washington
New Jersey	Earl J. Halligan, M.D., Jersey City
Upper New York	L. Pulsifer, M.D., Rochester
Tennessee	Ralph R. Braund, M.D., Memphis
Wisconsin	Robert T. McCarty, M.D., Milwaukee

PRELIMINARY PROGRAM

TWENTY-FOURTH ANNUAL CONVENTION AMERICAN COLLEGE OF GASTROENTEROLOGY

SCIENTIFIC SESSIONS 21, 22, 23 SEPTEMBER 1959

AND

COURSE IN POSTGRADUATE GASTROENTEROLOGY 24, 25, 26 SEPTEMBER 1959

THE BILTMORE HOTEL 515 SOUTH OLIVE STREET LOS ANGELES, CALIFORNIA

HAWAII REGIONAL MEETING 27 SEPTEMBER 1959

GENERAL INFORMATION

REGISTRATION—All members and guests should register. Identification badges for admittance to meetings will be given to those who register. These should be worn at all times during the session. Registration will take place at the registration desk on the convention floor. Registration facilities will open at 1:00 P.M. on Sunday and at 8:30 each morning.

LADIES REGISTRATION—At the registration desk on the Convention Floor. Registration facilities will open at 11:00 A.M. on Sunday and at 8:30 each morning. Information concerning the various activities and events will be available there.

DINNER-DANCE—Tickets will be sold by tables and will be available at the registration desk. Those desiring to be seated together must purchase tickets at the same time.

MEETINGS are held on local time and will begin promptly at the time specified.

COURSE IN POSTGRADUATE GASTROENTEROLOGY—Admittance only upon presentation of official matriculation card.

SCIENTIFIC EXHIBITS—Will be in the Exhibit Hall and will be open Monday, Tuesday, and Wednesday 8:30 a.m. to 5 p.m., Thursday from 8:30 a.m. to 1:00 p.m.

TECHNICAL EXHIBITS under the direction of Mr. Steven K. Herlitz, Exhibit Manager, will be open Monday, Tuesday, and Wednesday from 8:30 a.m. to 5:00 p.m., Thursday from 8:30 a.m. to 1:00 p.m.

HAWAII REGIONAL MEETING—Travel arrangements can be made through Travel Consultants, 1612 K St., N. W., Washington 6, D. C. or with their representative at the convention. There will be a $10.00 registration fee.

Those attending the Convention are urged to take advantage of the time in between the presentation of papers and sessions, to visit the technical exhibits and become acquainted with the many new products and new equipment on display.

SPEAKERS

ABRAMS, WILLIAM W., Ph.G., B.S., M.D., Kansas City, Kans. Chief, Gastroenterology, St. Margaret's Hospital; Chief, Metabolic Diseases, Providence Hospital.

BACHRACH, WILLIAM H., M.D., Los Angeles, Calif. Associate Clinical Professor of Medicine, University of Southern California School of Medicine.

BALFOUR, DONALD C., JR., M.S., M.D., San Marino, Calif. Assistant Clinical Professor of Medicine, University of Southern California School of Medicine.

BECK, L. CLAGGET, M.D., Honolulu, Hawaii.

BENNETT, L. R., M.D., Los Angeles, Calif. Associate Professor of Radiology, University of California at Los Angeles Medical Center.

BENZ, CHARLES C., B.S., M.D., Los Angeles, Calif. Hollywood Presbyterian Hospital; Olmsted Memorial.

BIDDLE, MARJORIE, B.A., Ph.D., Los Angeles, Calif. Visiting Assistant Professor of Microbiology, University of Southern California School of Medicine; Medical Microbiologist, Los Angeles County General Hospital.

BLUMENTHAL, LESTER S., M.D., M.S., Washington, D. C. Associate in Medicine, George Washington University School of Medicine; Director, Headache Clinic, George Washington University Hospital.

BOEHME, EARL J., M.D., Los Angeles, Calif. Assistant Professor of Surgery, College of Medical Evangelists, Los Angeles; Chief, Endocrine Surgery, White Memorial Hospital.

BORRELLI, FRANK J., M.D., F.A.C.G., New York, N. Y. Professor of Radiology, New York Medical College; Director of Radiology, Flower-Fifth Avenue Hospital.

BRODY, MELVIN, M.D., Los Angeles, Calif. Instructor in Medicine, University of California at Los Angeles Medical Center; Clinical Assistant in Gastroenterology, Veterans Administration Hospital.

BROWN, WILLIAM H., M.D., M.S., Los Angeles, Calif. Radiologist, Hollywood Presbyterian Hospital.

BULGRIN, JAMES G., M.D., Los Angeles, Calif. Assistant Clinical Professor of Radiology, University of Southern California School of Medicine; Attending Radiologist, Los Angeles County General Hospital.

BUZAID, LOUIS L., M.D., Honolulu, Hawaii. Director, Department of Radiology, The Queen's Hospital.

CAMP, JOHN D., Ch.B., M.D., F.A.C.R., Los Angeles, Calif. Clinical Professor of Radiology, University of Southern California School of Medicine; Chief, Department of Radiology, Hospital of The Good Samaritan.

CHANG, RICHARD, K.C., M.D., Honolulu, Hawaii. Consultant in Gastroenterology, The Queen's Hospital.

CIVIN, W. HAROLD, M.D., Honolulu, Hawaii.

COHEN, THEODORE, M.B., M.D., F.A.C.G., Forest Hills, N. Y. Instructor in Clinical Medicine, New York University-Post-Graduate Medical School; Research Associate, Brooklyn Hebrew Home and Hospital for the Aged; Assistant Visiting Physician, Bellevue Hospital; Assistant in Medicine, University Hospital.

CREEK, DALE W., A.B., M.D., F.A.C.G., Santa Barbara, Calif. Medical Staff, The Sansum Medical Clinic, Santa Barbara Cottage, Santa Barbara General and St. Francis Hospitals.

DAVIS, F. E., M.D., Los Angeles, Calif. Associate Clinical Professor of Pathology, University of Southern California School of Medicine; Pathologist, Hollywood Presbyterian Hospital; Attending Pathologist, Los Angeles County General Hospital.

DAVIS, HARRY A., M.D., Ph.D., Los Angeles, Calif. Senior Attending Surgeon, Los Angeles County General and California Hospitals.

DE CARVALHO, SERGIO, M.D., Ph.D., Cleveland Heights, Ohio. Director, Cancer Research, Rand Development Co.

DE HAY, RAYMOND M., M.D., Lanikai, Hawaii. Chief of Gastroscopy; Consultant Gastroenterologist; Chief, Gastrointestinal Clinic, St. Francis Hospital.

DELAMATER, JAMES N., A.B., M.D., F.A.C.P., Pasadena, Calif. Clinical Professor of Medicine, University of Southern California School of Medicine; Senior Attending, Los Angeles County General, Huntington Memorial and Arcadia Methodist Hospitals.

DE LA RIVA, XAVIER, M.D., F.A.C.G., Mexico, D.F. Professor, Postgraduate Courses; Chief, Out-Patient Clinic, General Hospital of Mexico.

DICKSON, D. R., M.D., Santa Barbara, Calif. Pathologist, Santa Barbara Cottage Hospital.

DOANE, WILTON A., B.S., M.D., F.A.C.S., Santa Barbara, Calif. Chief of Surgical Staff, St. Francis Hospital Teaching Staff, Santa Barbara Cottage Hospital.

DOMZ, C. A., M.D., F.A.C.G., Santa Barbara, Calif.

DUBOIS, EDMUND L., A.B., M.D., Beverly Hills, Calif. Assistant Clinical Professor of Medicine, University of Southern California School of Medicine.

ECKER, JEROME A., M.D., F.A.C.P., F.A.C.G., Santa Barbara, Calif. Chief of Medical Service, Santa Barbara Clinic.

FARRAR, TURLEY, M.D., M.S., Memphis, Tenn. Instructor in Surgery, University of Tennessee College of Medicine; Active Staff, Baptist Memorial Hospital.

FARRIS, JACK M., A.B., B.Sc., M.D., Los Angeles, Calif. Associate Clinical Professor of Surgery, University of California at Los Angeles Medical Center; Consultant, Veterans Administration.

FERGUSON, LYNN A., M.D., F.A.C.G., Grand Rapids Mich. Chief, Surgical Division, Ferguson-Droste-Ferguson Clinic and Hospital; Consulting Surgeon, Blodgett, St. Mary's and Butterworth Hospitals.

FIELD, JOHN B., B.S., Ph.C., M.S., Ph.D., M.D., Beverly Hills, Calif. Assistant Clinical Professor of Medicine, University of Southern California School of Medicine.

FRANKLAND, MARJORIE V., A.B., Los Angeles, Calif.

FRIEDEN, JULIAN H., M.D., Beverly Hills, Calif. Instructor in Surgery, University of California at Los Angeles Medical Center.

FUCHS, MARVIN, M.D., Washington, D.C. Associate in Medicine, George Washington University School of Medicine.

GITMAN, LEO, M.D., F.A.C.P., Brooklyn, N. Y. Director of Research, Brooklyn Hebrew Home and Hospital for the Aged.

GORDON, MARTIN E., M.D., New Haven, Conn.

GRANET, EMIL, M.D., F.A.C.G., New York, N. Y. Attending Surgeon (Proctology), Sea View Hospital; Assistant Attending Surgeon (Proctology), French Hospital; Assistant Attending Physician (Proctology), Elmhurst General Hospital.

GREANEY, EDWARD M., JR., B.S., M.D., North Hollywood, Calif. Instructor, Department of Surgery, University of Southern California School of Medicine; Junior Attending, Los Angeles Childrens Hospital.

GROTJAHN, MARTIN, M.D., Beverly Hills, Calif. Assistant Clinical Professor of Psychiatry, University of Southern California School of Medicine; Consultant, Veterans Administration Hospital.

GUTH, PAUL H., B.S., M.D., Orange, Calif. Instructor in Medicine, University of Southern California School of Medicine; Director of Gastroenterology, Orange County General Hospital.

HAUCH, EDWARD W., B.A., M.S., M.D., F.A.C.P., Pomona, Calif. Assistant Clinical Professor of Medicine (Gastroenterology), University of Southern California School of Medicine; Chief of Medical Department, Pomona Valley Community Hospital; Attending Staff, Los Angeles County General and Pomona Valley Community Hospitals.

HAVERBACK, BERNARD J., M.D., Los Angeles, Calif. Assistant Professor of Medicine, University of Southern California School of Medicine.

HEALEY, LOUIS A., M.D., Seattle, Wash. Resident in Medicine, University of Washington Medical School.

HEINEKEN, THEODORE S., M.D., F.A.C.P., F.A.C.G., Glen Ridge, N. J. Attending, Mountainside Hospital; Consultant Gastroenterologist, Clara Maas Hospital.

HOAG, C. L., B.S., Santa Barbara, Calif.

HOLLERAN, WALTER M., M.D., Los Angeles, Calif. Staff Surgeon, Queen of Angels Hospital.

IVES, ELINOR R., B.A., M.D., Los Angeles, Calif. Assistant Clinical Professor, University of Southern California School of Medicine; Attending, Los Angeles County General Hospital; Consultant in Neurology, Veterans Administration Regional Office; Consultant, California State Hospital.

KNIGHTS, JOHN A., M.D., Santa Barbara, Calif. Chief, Department of Radiology, Sansum Medical Clinic.

LICHSTEIN, JACOB, M.D., F.A.C.P., F.A.C.G., Los Angeles, Calif. Assistant Professor of Clinical Medicine, University of Southern California School of Medicine; Attending, Cedars of Lebanon Hospital.

MAGID, GEORGE J., B.A., M.D., Seattle, Wash. Clinical Instructor in Medicine, University of Washington Medical School; Attending Staff, King County, Veterans Administration and University of Washington Hospitals.

McDONALD, JOHN B., M.D., F.A.C.G., Beverly Hills, Calif. Hollywood Presbyterian and St. John's Hospitals.

MARKEES, SYLVIO, M.D., Ph.D., Basel, Switzerland. Research Department, Hoffmann-La Roche.

MELLINKOFF, SHERMAN M., M.D., Los Angeles, Calif. Associate Professor of Medicine, University of California at Los Angeles Medical Center.

MENA, ISMAEL, M.D., Los Angeles, Calif. Associate Research Endocrinologist, University of California at Los Angeles Medical Center.

MIKULICICH, GEORGE F., M.D., Alhambra, Calif. University of Southern California School of Medicine.

MOHR, GEORGE J., B.A., M.D., Los Angeles, Calif. Clinical Professor of Psychiatry, University of Southern California School of Medicine; Director, Division of Child Psychiatry, Mt. Sinai Hospital.

MOLANDER, DAVID W., B.S., M.D., M.S., New York, N. Y. Instructor in Medicine, Cornell University Medical School; Department of Medicine, Memorial Hospital.

MONTANEZ, OCTAVIO, M.D., F.I.A.P., F.A.C.G., Mexico, D.F. Professor, Graduate Medical School, National University of Mexico; Chief, Surgical Department, Hospital Central S.C.T.

MORRISON, LESTER M., M.D., F.A.C.P., F.A.C.G., Los Angeles, Calif. Lecturer in Medicine, College of Medical Evangelists; Senior Attending Physician, Los Angeles County General Hospital.

MOYER, DEAN L., Pacific Palisades, Calif. Instructor of Pathology, University of California at Los Angeles Medical Center.

MULDER, DONALD G., M.D., Los Angeles, Calif. Assistant Professor of Surgery, University of California at Los Angeles Medical Center.

OETTING, HENRY K., A.B., M.D., Los Angeles, Calif. Assistant in Medicine, University of Southern California School of Medicine.

PACK, GEORGE T., M.D., New York, N. Y. Associate Clinical Professor of Medicine, Cornell University Medical School; Department of Surgery, Memorial Hospital.

PERRY, JOHN W., M.D., Hollywood, Calif. Hollywood Presbyterian Hospital.

POWSNER, L. G., Los Angeles, Calif. Staff Surgeon, Queen of Angels Hospital.

PROPATORIDIS, JORDAN T., M.D., F.A.C.G., Athens, Greece. Chief, Second Surgical Clinic, General State Hospital of Athens.

PUENTE PEREDA, FRANCISCO, B.S., M.D., F.A.C.S., F.A.C.G., Mexico, D.F. Professor of Surgery, University of Mexico; Chief of Gastroenterology, Sanatorio Hacienda; Chief of Surgery, La Raza Hospital.

REDEKER, ALLAN G., M.D., Los Angeles, Calif. Instructor in Medicine, University of Southern California School of Medicine.

RIMER, DAVID G., M.D., Los Angeles, Calif. Instructor in Medicine, University of California at Los Angeles Medical Center.

ROEN, PAUL B., M.D., F.A.C.P., Los Angeles, Calif. Hollywood Presbyterian Hospital.

ROSS, DONALD E., M.D., F.A.C.S., F.A.C.G., Los Angeles, Calif. Teaching Staff, Queen of Angels Hospital; Chief Surgeon, Ross-Loos Medical Group.

ROWE, ALBERT H., B.S., M.S., M.D., Oakland, Calif. Lecturer in Medicine (Emeritus), University of California; Allergist, Merritt and Oakland Naval Hospitals.

ROWE, ALBERT, JR., M.D., Oakland, Calif. Assistant Physician, Highland Hospital.

SANDERS, L. CARL, M.D., F.A.C.P., F.A.C.G., Memphis, Tenn. Associate Professor of Medicine, University of Tennessee College of Medicine; Senior Staff, Baptist Memorial Hospital.

SCHWABE, ARTHUR, A. B., M.D., Los Angeles, Calif. Fellow in Gastroenterology, University of California at Los Angeles Medical Center.

SIDENBERG, STANLEY S., M.D., F.A.C.G., Cleveland, Ohio. Visitant in Medicine, Mt. Sinai, Doctors and Suburban Community Hospitals.

STARR, PAUL, M.D., F.A.C.G. (Hon.), Pasadena, Calif. Emeritus Professor, University of Southern California School of Medicine; Active Consultant, Los Angeles County General Hospital; Research-Attending Staff Association, Los Angeles County General Hospital.

STEIGMANN, FREDERICK, M.D., M.S., F.A.C.G., Chicago, Ill. Associate Professor of Medicine, University of Illinois College of Medicine; Chief of Gastroenterology and Attending Physician, Cook County Hospital.

STOWENS, DANIEL, A.B., M.D., Los Angeles, Calif. Associate Professor of Pathology, University of Southern California School of Medicine; Pathologist and Director of Experimental Pathology, Children's Hospital.

THOMAS, H. V., A.B., M.S., Los Angeles, Calif. Researcher, University of Southern California School of Medicine.

F.A.C.G., Long Beach, Calif. Chief of Staff, Seaside Memorial Hospital; Attending Surgeon, Los Angeles County Harbor General Hospital.

TOOL, HARRY, M.D., Athens, Greece. Clinical Professor of Surgery, University of Athens Medical School.

TREUSCH, JEROME V., M.D., F.A.C.P., Beverly Hills, Calif. Assistant Clinical Professor of Medicine, University of Southern California School of Medicine; Senior Attending Physician, Los Angeles County General Hospital.

VICTOROFF, VICTOR, M.D., Cleveland, Ohio. Visiting Neuropsychiatrist, Doctors, Women's, and Windsor Hospitals.

WAITE VERNE C., M.D., Honolulu, Hawaii.

WALLACE, ALEXANDER, III, M.D., M.S., F.A.C.G., Los Angeles, Calif. Instructor in Medicine, University of Southern California School of Medicine.

WEINGARTEN, BERTHOLD, M.D., F.A.C.G., New York, N. Y. Assistant Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons; Physician, Montefiore Hospital.

WEISS, BERNARD, M.D., New York, N. Y.

WEISS, JEROME, B.S., M.D., F.A.C.G., New York, N. Y. Lecturer, Polyclinic Medical School and Hospital; Adjunct in Medicine, Montefiore Hospital; Attending Gastroenterologist, Polyclinic Medical School and Hospital, OPD; Associate Physician (Gastroscopy), Goldwater Hospital; Assistant Attending Polyclinic Medical School and Hospital.

WEISS, SAMUEL, M.D., Sc.D. (Hon.), F.A.C.P., F.A.C.G., New York, N. Y. Emeritus Professor of Gastroenterology, Polyclinic Medical School and Hospital; Consultant Gastroenterology, Jewish Memorial, Grand Central and Long Beach Memorial Hospitals.

WHARTON, GEORGE K., M.D., M.S., F.A.C.G., Los Angeles, Calif. Professor of Clinical Medicine (Gastroenterology), University of Southern California School of Medicine.

WIRTS, C. WILMER, B.S., M.D., F.A.C.G., Philadelphia, Pa. Associate Professor of Medicine and Director, Division of Gastroenterology, The Jefferson Medical College and Hospital.

Business Sessions

SATURDAY, 19 SEPTEMBER 1959

All Day

Various committee meetings at times to be arranged by committee chairmen—Conference Room 7.

SUNDAY, 20 SEPTEMBER 1959

9:00 A.M.

Annual Meeting of the Board of Trustees—Conference Room 8.

1:00 P.M.

Luncheon, Board of Trustees and Board of Governors—Conference Room 4.

3:00 P.M.

Annual Meeting of the American College of Gastroenterology—Conference Room 1.

4:45 P.M.

Convocation Rehearsal (without caps and gowns)—Renaissance Room.

6:30 P.M.

CONVOCATION: Presentation of Certificates—Renaissance Room. See special program.

8:30 P.M.

Buffet Supper—Music Room. Sponsored by William H. Rorer, Inc. (Admission by card only, to be obtained at the Convocation Ceremony).

9:30 P.M.

Motion Picture: "Wild Flowers of the West" in color, Courtesy of the Richfield Oil Corp. —Music Room.

MONDAY, 21 SEPTEMBER 1959

5:00 P.M.

Meeting of the Credentials Committee—Conference Room 6.

TUESDAY, 22 SEPTEMBER 1959

12:30 P.M.

Annual Meeting and Luncheon of the Board of Governors—Conference Room 4.

WEDNESDAY, 23 SEPTEMBER 1959

12:30 P.M.

Luncheon Meeting of the Board of Trustees —Conference Room 4.

SCIENTIFIC SESSIONS

FIRST SESSION

MONDAY MORNING,
21 SEPTEMBER 1959

8:30–9:30 A.M. *Coffee and sweet rolls will be served in the Exhibit Area with the compliments of the House of Seagram.*

FRANK J. BORRELLI, M.D., F.A.C.G., President, American College of Gastroenterology, presiding.

9:00 A.M.

1. Water-Electrolyte Disturbances in Gastrointestinal Disease.

Speaker

DR. HARRY A. DAVIS, Los Angeles, Calif. (By invitation).

9:15 A.M.

2. Pitfalls in Fluoroscopy and Radiography of the Esophagus.

Speaker

DR. CHARLES C. BENZ, Los Angeles, Calif. (By invitation).

9:30 A.M.

3. Hiatus Hernia.

Speakers

DR. L. CARL SANDERS, Memphis, Tenn. and DR. TURLEY FARRAR, Memphis, Tenn.

9:45 A.M.

4. Changing Indications for Surgery in Peptic Ulcer.

Speaker

DR. WILLIAM H. BACHRACH, Los Angeles, Calif. (By invitation).

10:00 A.M.

Discussion of Papers 1-4.

Discussers

DR. BERT COTTON, Los Angeles Calif. (By invitation) and DR. FRANK J. BORRELLI, New York, N. Y.

10:30 A.M. Recess to visit the commercial, technical and scientific exhibits.

11:00 A.M.

5. A Critical Review of 900 Cases of Gastroduodenal Surgery.

Speakers

DR. L. G POWSNER, Los Angeles, Calif. (By invitation), DR. DONALD E. ROSS, Los Angeles, Calif. and DR. WALTER M. HOLLERAN, Los Angeles, Calif. (By invitation).

11:15 A.M.

6. Gastric Resections in Mexico.

Speakers

DR. F. PUENTE PEREDA, Mexico, D.F. and DR. XAVIER DE LA RIVA, Mexico, D.F.

11:30 A.M.

Discussion of papers 5 and 6.

Discussers

DR. ROBERT GOLDEN, Los Angeles, Calif. (By invitation) and DR. HAROLD L. THOMPSON, Los Angeles, Calif. (By invitation).

11:45 A.M.

7. HENRY G. RUDNER, SR. AWARD PAPER.

The Acute Effects of Abdominal Paracentesis in Laennec's Cirrhosis Upon Exchanges of Electrolytes and Water, Renal Function and Hemodynamics.

Speaker

DR. MARTIN E. GORDON, New Haven, Conn.

12:30 P.M.

LUNCHEON – Sponsored by Burton, Parsons & Co. – Renaissance Room. (admission by card only, to be obtained at the registration desk).

SECOND SESSION

MONDAY AFTERNOON,
21 SEPTEMBER 1959

HENRY BAKER, M.D. F.A.C.G., Vice-President, American College of Gastroenterology, presiding.

2:00 P.M.

8. Tranquilizers and Gastric Secretion: With Comments on Clinical Experience in 60 Cases when Combined with Anticholinergic Drugs in Gastrointestinal Disease.

Speakers

DR. JACOB LICHSTEIN, Los Angeles Calif. and HERIBERTO V. THOMAS, Los Angeles, Calif. (By invitation).

2:15 P.M.

9. Antacids in Peptic Ulcer. 1. Biochemical and Economic Considerations.

Speaker

DR. MELVIN BRODY, Los Angeles, Calif. (By invitation).

2:30 P.M.

10. The Sodium Content of Antacids.

Speakers

DR. DAVID G. RIMER, Los Angeles, Calif. (By invitation), Marjorie V. Frankland, Los Angeles, Calif. (By invitation) and DR. SHERMAN M. MELLINKOFF, Los Angeles, Calif. (By invitation).

2:45 P.M.

11. Sublingual and Suppository Therapy in Internal Medicine.

Speakers

DR. LESTER S. BLUMENTHAL, Washington, D.C. (By invitation) and DR. MARVIN FUCHS, Washington, D.C. (By invitation).

3:00 P.M.
Discussion of papers 8-11.

Discussers

DR. CLINTON S. THIENES. Pasadena, Calif. (By invitation) and DR. JOHN L. WEBB, Los Angeles, Calif. (By invitation).

3:30 P.M. Recess to visit the commercial, technical and scientific exhibits.

4:00 P.M.

12. The Use of Cytology in Gastroenterology.

Speaker

DR. DEAN L. MOYER, Pacific Palisades, Calif. (By invitation).

4:15 P.M.

13. Malignant Degeneration in Chronic Inflammatory Disease of the Colon and Small Intestine.

Speakers

DR. BERTHOLD WEINGARTEN, New York, N. Y. and DR. JEROME WEISS, New York, N. Y.

4:30 P.M.

Discussion of papers 12 and 13.

Discussers

DR. MILTON ROSENTHAL, Los Angeles, Calif. (By invitation) and DR. LESTER M. MORRISON, Los Angeles, Calif.

6:30-8:30 P.M.

President's Reception and Cocktail Party in honor of Dr. Andrew Muir — Sponsored by Smith-Dorsey — (admission by invitation only, to be obtained at the registration desk).

THIRD SESSION

TUESDAY MORNING,
22 SEPTEMBER 1959

8:30-9:30 A.M. *Coffee and sweet rolls will be served in the Exhibit Area with the compliments of the House of Seagram.*

LOUIS OCHS, JR., M.D., F.A.C.G., Vice-President, American College of Gastroenterology, presiding.

9:00 A.M.

14. Needle Biopsy of the Liver in Infancy and Early Childhood.

Speaker

DR. DANIEL STOWENS, Los Angeles, Calif. (By invitation).

9:15 A.M.

15. The Role of Surgery in the Treatment of Portal Hypertension.

Speaker

DR. DONALD G. MULDER, Los Angeles, Calif. (By invitation).

9:30 A.M.

16. Combined Use of I^{131} and BSP in the Study of Liver Function.

Speakers

DR. L. R. BENNETT, Los Angeles, Calif. (By invitation), DR. ISMAEL MENA, Los Angeles, Calif. (By invitation) and DR. SHERMAN M. MELLINKOFF, Los Angeles, Calif. (By invitation).

9:45 A.M.

17. Physiological Studies and Management of Patients Undergoing Total Hepatic Lobectomy.

Speakers

DR. DAVID W. MOLANDER, New York, N. Y. (By invitation) and DR. GEORGE T. PACK, New York, N. Y. (By invitation).

10:00 A.M.

Discussion of papers 14-17.

Discussers

DR. W. P. MIKKELSEN, Los Angeles, Calif. (By invitation) and DR. S. AUSTIN JONES, Los Angeles, Calif. (by invitation).

10:30 A.M. Recess to visit the commercial, technical and scientific exhibits.

11:00 A.M.

18. The Ominous Reciprocity Between Liver Disease and Pancreatitis.

Speaker

DR. FREDERICK STEIGMANN, Chicago, Ill.

11:15 A.M.

19. Evaluation of Phototurbidimetric Technics for the Determination of Serum Amylase, Lipase and Esterase.

Speaker

DR. PAUL H. GUTH, Orange, Calif. (By invitation).

11:30 A.M.

Discussion of papers 18 and 19.

Discussers

DR. A. G. WARE, Los Angeles, Calif. (By invitation) and DR. SHERMAN M. MELLINKOFF, Los Angeles, Calif. (By invitation).

FOURTH SESSION

TUESDAY AFTERNOON,
22 SEPTEMBER 1959

EDWARD J. KROL, M.D., F.A.C.G., Vice-President, American College of Gastroenterology, presiding.

2:00 P.M.

20. Diagnosis and Treatment of Duodenal Diverticula.

Speaker

DR. THEODORE S. HEINEKEN, Glen Ridge, N. J.

2:15 P.M.

21. The Management of Acute Proctologic Conditions.

Speaker

DR. EMIL GRANET, New York, N. Y.

2:30 P.M.

22. Clinical Evaluation of the Gastrointestinal Tract in the Aged.

Speakers

DR. THEODORE COHEN, Forest Hills, N. Y. and DR. LEO GITMAN, Brooklyn, N. Y. (By invitation).

2:45 P.M.

23. Gastrointestinal Bleeding in Hereditary Hemorrhagic Telangiectasia.

Speakers

DR. JEROME A. ECKER, Santa Barbara, Calif., DR. WILTON A. DOANE, Santa Barbara, Calif. (By invitation) and DR. DELBERT DICKSON, Santa Barbara, Calif. (By invitation).

3:00 P.M.

Discussion of papers 20-23.

Discussers

Dr. Arthur A. Kirchner, Los Angeles, Calif. and Dr. Fred E. Bradford, Los Angeles, Calif. (By invitation).

3:30 P.M. Recess to visit the commercial, technical and scientific exhibits.

4:00 P.M.

24. Brief Review of the Enterohepatic Metabolism of Thyroxine.

Speaker

Dr. Paul Starr, Pasadena, Calif.

4:15 P.M.

25. The Problem of the Corticosteroid Induced Ulcer.

Speakers

Dr. Edmund L. Dubois, Beverly Hills, Calif. (By invitation) and Dr. James G. Bulgrin, Los Angeles, Calif. (By invitation).

4:30 P.M.

Discussion of papers 24 and 25.

Discussers

Dr. C. Wilmer Wirts, Philadelphia, Pa. and Dr. Douglas R. Drury, Los Angeles, Calif. (By invitation).

7:00 P.M.

ANNUAL DINNER DANCE—RENAISSANCE ROOM, The Biltmore Hotel, Los Angeles, Calif.

FIFTH SESSION

WEDNESDAY MORNING,
23 SEPTEMBER 1959

8:30-9:30 A.M. *Coffee and sweet rolls will be served in the Exhibit Area with the compliments of the House of Seagram.*

THEODORE S. HEINEKEN, M.D., F.A.C.G., Vice-President, American College of Gastroenterology, presiding.

9:00 A.M.

26. The New Laboratory Test for Viral Hepatitis.

Speaker

Dr. Lester M. Morrison, Los Angeles, Calif.

9:15 A.M.

27. A Comparative Study of Hydrochlorothiazide and Chlorothiazide on Blood Ammonia and Electrolyte Balance in Cirrhotic Patients.

Speakers

Dr. George J. Magid, Seattle, Wash. (By invitation) and Dr. Louis A. Healey, Seattle, Wash. (By invitation).

9:30 A.M.

28. Diabetic-Ketogenesis in Experimental Liver Damage.

Speakers

Dr. George F. Mikulicich, Alhambra, Calif. (By invitation) and Dr. Sylvia Markees, Basel, Switzerland (By invitation).

9:45 A.M.

29. The Surgical Treatment of Prolapse of the Gastric Mucosa.

Speaker

Dr. Malcolm C. Todd, Long Beach, Calif.

10:00 A.M.

Discussion of papers 26-29.

Discussers

Dr. E. Geiger, Los Angeles, Calif. (By invitation) and Dr. Jacob Lichstein, Los Angeles, Calif.

10:30 A.M. Recess to visit the commercial, technical and scientific exhibits.

11:00 A.M.

30. A New Technic of Psychosomatic Consultations.

Speakers

Dr. Martin Grotjahn, Beverly Hills, Calif. (By invitation) and Dr. Jerome V. Treusch, Beverly Hills, Calif. (By invitation).

11:15 A.M.

31. Problems in Patient Management Following Gastric Surgery.

Speaker

Dr. C. Wilmer Wirts, Philadelphia, Pa.

11:30 A.M.

Discussion of papers 30 and 31.

Discussers

Dr. Edward M. Butt, Los Angeles, Calif. (By Invitation), Dr. Karem J. Monsour, Pasadena, Calif. (By invitation) and Dr. George N. Thompson, Los Angeles, Calif. (By invitation).

SIXTH SESSION

WEDNESDAY AFTERNOON,
23 SEPTEMBER 1959

DALE W. CREEK, M.D., F.A.C.G., Chairman, Board of Governors, American College of Gastroenterology, presiding.

2:00 P.M.

32. The Mallory-Weiss Syndrome.

Speaker

Dr. William W. Abrams, Kansas City, Kansas.

2:15 P.M.

33. Serum Trypsin Inhibitors in Pancreatitis.

Speaker

Dr. Bernard J. Haverback, Los Angeles, Calif. (By invitation).

2:30 P.M.

34. Familial Mediterranean Fever.

Speakers

Dr. Arthur Schwabe, Los Angeles, Calif. (By invitation) and Dr. Sherman M. Mellinkoff, Los Angeles, Calif. (By invitation).

2:45 P.M.

35. Porphyria — A Disease of the Liver and Liver Enzymes.

Speakers

Dr. Sergio De Carvalho, Cleveland Heights, Ohio (By invitation), Dr. Victor Victoroff, Cleveland, Ohio (By invitation) and Dr. Stanley S. Sidenberg, Cleveland, Ohio.

3:00 P.M.

Discussion of papers 32-35.

Discussers

Dr. H. Bundy, Los Angeles, Calif. (By invitation) and Dr. John B. McDonald, Beverly Hills, Calif.

3:30 P.M. Recess to visit the commercial, technical and scientific exhibits.

4:00 P.M.

36. The Effect of Safflower Oil on Serum Lipids.

Speakers

Dr. John B. McDonald, Beverly Hills, Calif., Dr. Paul B. Roen, Los Angeles, Calif. (By invitation) and Dr. John W. Perry, Hollywood, Calif.

4:15 P.M.

37. The Effects of Iproniazide and Similar Compounds on the Gastrointestinal Tract (A Clinical Evaluation).

Speakers

Dr. Jerome Weiss, New York, N. Y., Dr. Samuel Weiss, New York, N. Y., and Dr. Bernard Weiss, New York, N. Y.

4:30 P.M.

38. Some Statistical and Other Interesting Remarks Concerning the Gastroduodenal Ulcer in Greece.

Speakers

Dr. Jordan Propatoridis, Athens, Greece and Dr. Harry Tool, Athens, Greece (By invitation).

4:45 P.M.

Discussion of papers 36-38.

Discusser

Dr. Thomas H. Brem, Los Angeles, Calif. (By invitation).

COURSE IN POSTGRADUATE GASTROENTEROLOGY

FIRST SESSION

THURSDAY MORNING,
24 SEPTEMBER 1959

Attendance at the Postgraduate Course is limited to those who have registered and paid the matriculation fee.

8:30-9:30 A.M.—*Coffee and sweet rolls will be served in the Exhibit Area with the compliments of the House of Seagram.*

JULIUS BAUER, M.D. and HARRY DAVIS M.D., *Moderators.*

9:00 A.M.

Address of Welcome—JOSEPH SHAIKEN, M.D., F.A.C.G., President, American College of Gastroenterology.

9:05 A.M.

1. Some Recent Aspects of Fat Metabolism.

Speakers

H. V. THOMAS, Altadena, Calif., and DR. GEORGE K. WHARTON, Los Angeles, Calif.

9:25 A.M.

2. Gastrointestinal Bleeding in the Cirrhotic.

Speaker

DR. HENRY K. OETTING, Los Angeles, Calif.

9:45 A.M.

3. Accuracy of Serum Pepsinogen in the Diagnosis of Duodenal Ulcer as Compared to Ewald and Diagnex Tests.

Speakers

DR. C. A. DOMZ, Santa Barbara, Calif. and C. L. HOAG, Santa Barbara, Calif.

10:05 A.M.

4. Recent Advances in Roentgenology of the Upper Gastrointestinal Tract.

Speaker

DR. JOHN D. CAMP, Los Angeles Calif.

10:25 A.M.

Discussion of papers 1-4.

10:45 A.M. Recess to visit the commercial, technical and scientific exhibits. (Exhibits close at 1:00 P.M.).

11:15 A.M.

5. PANEL DISCUSSION ON GASTRIC ULCER IN 1959.

Moderator

DR. DALE W. CREEK, Santa Barbara, Calif.

Participants:

DR. D. R. DICKSON, Santa Barbara, Calif.
DR. WILTON A. DOANE, Santa Barbara, Calif.
DR. C. A. DOMZ, Santa Barbara, Calif.
DR. JEROME A. ECKER, Santa Barbara, Calif.
DR. JOHN A. KNIGHTS, Santa Barbara, Calif.

SECOND SESSION

THURSDAY AFTERNOON,
24 SEPTEMBER 1959

Attendance at the Postgraduate Course is limited to those who have registered and paid the matriculation fee.

This entire session will be held in the amphitheater at the White Memorial Hospital, 315 North Bailey Street.

2:30 P.M.

6. Clinical Session.

THIRD SESSION

FRIDAY MORNING,
25 SEPTEMBER 1959

Attendance at the Postgraduate Course is limited to those who have registered and paid the matriculation fee.

This session and all subsequent sessions will again be held at the Biltmore Hotel.

CLARENCE J. BERNE, M.D., and STEPHEN J. STEMPIEN, M.D., *Moderators.*

9:00 A.M.

7. Chemotherapy for Malignancies of the Gastrointestinal Tract.

Speaker

DR. JOHN B. FIELD, Beverly Hills, Calif.

9:20 A.M.

8. Differential Diagnosis of Jaundice.

Speaker

Dr. Alexander Wallace, III, Los Angeles, Calif.

9:40 A.M.

9. Problems in the Diagnosis of Acute Porphyria.

Speaker

Dr. Allan G. Redeker, Los Angeles, Calif.

10:00 A.M.

Discussion of papers 7-9.

10:30 A.M. Recess

10:45 A.M.

10. PANEL DISCUSSION ON LIVER DISEASE.

Moderator

Dr. Donald C. Balfour, Jr., San Marino, Calif.

Participants:

Dr. Bernard J. Haverback, Los Angeles, Calif.
Dr. Sherman M. Mellinkoff, Los Angeles, Calif.
Dr. Allan G. Redeker, Los Angeles, Calif.
Dr. Alexander Wallace, III. Los Angeles, Calif.

12:15 P.M.

BUFFET LUNCHEON — Renaissance Room (Admission by card only).

FOURTH SESSION

FRIDAY AFTERNOON,
25 SEPTEMBER 1959

Attendance at the Postgraduate Course is limited to those who have registered and paid the matriculation fee.

Clarence J. Berne, M.D., and Stephen J. Stempien, M.D., *Moderators.*

1:30 P.M.

11. The Gastrointestinal Tract as the Target of Neurologic Disease.

Speaker

Dr. Elinor R. Ives, Los Angeles, Calif.

1:50 P.M.

12. Psychological Aspects of Ulcerative Colitis.

Speaker

Dr. George J. Mohr, Los Angeles, Calif.

2:10 P.M.

13. Chronic Ulcerative Colitis Relieved by Antiallergic Therapy.

Speakers

Dr. Albert H. Rowe, Oakland, Calif. and Dr. Albert Rowe, Jr., Oakland, Calif.

2:30 P.M.

Discussion of papers 11-13.

3:00 P.M. Recess

3:10 P.M.

14. Chronic Ulcerative Colitis as Viewed by the Internist.

Speaker

Dr. Edward W. Hauch, Pomona, Calif.

3:30 P.M.

15. Chronic Nonspecific Ulcerative Colitis — Roentgen Manifestations and Response to Medical Management.

Speakers

Dr. William H. Brown, Los Angeles, Calif. and Dr. George K. Wharton, Los Angeles, Calif.

3:50 P.M.

16. Surgical Cure of Ulcerative Colitis.

Speaker

Dr. Earl J. Boehme, Los Angeles Calif.

4:10 P.M.

17. Pathology of Ulcerative Colitis.

Speaker

Dr. F. E. Davis, Los Angeles, Calif.

4:30 P.M.

Discussion of papers 14-17.

FIFTH SESSION

SATURDAY MORNING,
26 SEPTEMBER 1959

Attendance at the Postgraduate Course is limited to those who have registered and paid the matriculation fee.

JOHN KESSEL, Ph.D. and CLAYTON LOOSLI, M.D., Ph.D., *Moderators.*

9:00 A.M.

18. Diagnosis of Intestinal Parasites.

Speakers

DR. MARJORIE BIDDLE, Los Angeles, Calif. and DR. GEORGE K. WHARTON, Los Angeles, Calif.

9:20 A.M.

19. Treatment of Alimentary Worm Infestations.

Speaker

DR. JAMES N. DELAMATER, Pasadena, Calif.

9:40 A.M.

20. Amebic Liver Abscess Ruptured Into Digestive Tube.

Speaker

DR. OCTAVIO MONTANEZ, Mexico, D.F.

10:00 A.M.

Discussion of papers 18-20.

10:30 A.M. Recess.

10:45 P.M.

21. PANEL DISCUSSION ON PANCREATIC DISEASE.

Moderator

DR. DONALD E. ROSS, Los Angeles, Calif.

Participants:

DR. J. M. FARRIS, Los Angeles, Calif.
DR. JULIAN H. FRIEDEN, Beverly Hills, Calif.
DR. EDWARD M. GREANEY, JR., North Hollywood, Calif.
DR. PAUL H. GUTH, Orange, Calif.

HAWAII REGIONAL MEETING

FIRST SESSION

SUNDAY MORNING,
27 SEPTEMBER 1959

10:00 A.M.

1. Panel Discussion on Experience in Hawaii with Infections of the Colon.

DR. L. CLAGGET BECK, Honolulu, Hawaii.
DR. LOUIS L. BUZAID, Honolulu, Hawaii.
DR. RICHARD K. C. CHANG, Honolulu, Hawaii
DR. W. HAROLD CIVIN, Honolulu, Hawaii.
DR. RAYMOND M. DEHAY, Lanikai, Hawaii.
DR. VERNE C. WAITE, Honolulu, Hawaii.

SECOND SESSION

SUNDAY AFTERNOON,
27 SEPTEMBER 1959

2:00 P.M.

2. To Be Announced.

Speaker

DR. DALE W. CREEK, Santa Barbara, Calif.

2:15 P.M.

3. Experience with Factitial Proctitis.

Speaker

DR. LYNN A. FERGUSON, Grand Rapids, Mich.

2:30 P.M.

4. Panel Discussion.

Moderator

DR. FRANK J. BORRELLI, New York, N. Y.

Participants

DR. DALE W. CREEK, Santa Barbara, Calif.
DR. LYNN A. FERGUSON, Grand Rapids, Mich.

SCIENTIFIC EXHIBITS

Booth A

Aspirin and Gastric Damage

A. Muir, M.B., Ch.B., M.R.C.P.,
Lanarkshire, Scotland

This exhibit describes the results obtained in a comparative study between aspirin and calcium aspirin on the gastrointestinal tract. It consisted of the observation of the comparative effects of these products on the gastric mucosa of duodenal ulcer patients on whom gastrectomies have been performed. Color photographs will be presented to show the results that have been obtained. Fecal occult blood has been determined in patients who have received aspirin or calcium aspirin on an acute and chronic basis. These results will be presented. Normal subjects and patients with existing gastric disturbances have been administered caffeine and aspirin test meals. The comparative effects of aspirin and calcium aspirin will be presented. The results indicate that calcium aspirin produces less irritation than aspirin when measured on an objective basis.

Booth B

Pathophysiology, Diagnosis and Treatment of Esophageal Diseases

J. A. Rider, M.D., Ph.D. and Hugo C. Moeller, M.D., Ph.D., San Francisco, Calif.

This exhibit is devoted exclusively to the diagnosis and treatment of the common diseases of the esophagus. New diagnostic procedures will be shown. These include illustrations of the use of a safe, flexible esophagoscope, movies of the esophagus taken through the fluoroscopic screen, and illustrations of esophageal biopsy and cytological examinations used to diagnose esophageal cancer. Artists' drawings, x-rays and esophagoscopic views of various diseases will be shown. Specific treatment indicated for each disease condition will be stressed. An outstanding feature of the exhibit is the last panel, which shows by x-ray cinemafluoro-photography the esophagus before, during, and after esophageal dilatation with a special pneumatic esophageal dilator for the treatment of achalasia and cardiospasm.

Booth C

Psychogenic Megacolon

Paul S. Mahoney, M.D., Bernard J. O'Loughlin, M.D., Ph.D. and Charles Johnson, B.A., Los Angeles, Calif.

Psychogenic megacolon is an acquired disease of infancy found in children after 2 years of age. The disease is manifested by encopresis in children who demonstrate emotional problems secondary to cohesive bowel training.

The disease is characterized roentgenographically by children who are extremely stoic during a barium enema examination. The colon is dilated, redundant and elongated without evidence of an aganglionic segment. The child often will retain 98 per cent of barium after postevacuation study.

Surgery in these children is contraindicated. Psychotherapy of parents and children is the only means of treatment.

Booth D

Gastrointestinal Motility, Physiologic and Clinical Considerations

Jacob Lichstein, M.D., F.A.C.P., F.A.C.G. and J. Da Costa Mayer, M.D., Los Angeles, Calif.

The theme of the exhibit is the general subject of gastrointestinal motility. The presentation will consist of a description of methods of recording pressure and motility changes developed to date with tracings and photographs and additional attention to the new electronic and cinefluorographic devices (e.g. image amplifier). Basic physiologic concepts gradually evolved in recent years by these methods will be listed. The relationship of hypermotility and hypomotility to clinical syndromes met with in practice and factors contributing to disturbed physiologic function will be presented. Our knowledge of effects of pharmacologic agents on motility and general therapeutic approaches to the problem of disturbed motility with attention to the most common disorder, the irritable colon, will be dealt with. Mention will be made of the unanswered questions and problems to be explored in the future in this field.

Booth E

Control of Tension in General Surgery

TIMOTHY A. LAMPHIER, M.D., F.A.C.G., Boston, Mass.

The scope of the tension-anxiety-depression problem, in both the preoperative and postoperative patient, is reviewed, and the need for an effective relaxant is discussed. Results of tranquilizer/muscle relaxant (Meprobamate) therapy among more than 350 surgery patients are presented, which indicate that Meprobamate effectively relieves pre- and postoperative tension and is, therefore, a valuable adjunct in the management of the surgical patient.

No serious adverse reactions to the drug were observed among the patients. There were no "cumulative" effects; no effect on the autonomic nervous system; and no signs of addiction, habituation, withdrawal symptoms or tolerance.

Booth F

Use of Diatrizoate Sodium as Contrast Medium in Gastrointestinal Examination

BENJAMIN O. MORRISON, M.D., TIMOTHY J. HALEY, M.D., ARTHUR R. PAYZANT, M.D., GEORGE A. GENTNER, M.D. and J. PAGAN-CARLO, M.D., New Orleans, La.

Uses of an oral radiopaque medium (Hypaque) are described in gastrointestinal examinations, roentgenograms and esophagrams. Nonabsorbable and nontoxic, its somewhat bitter taste was disguised by mixing Hypaque with 6 oz. (180 c.c.) of grape juice. Hypaque was useful in children for suspected tracheoesophageal fistulas and pyloric stenosis. In adults, Hypaque was valuable in cases of pyloric and intestinal obstruction, bleeding gastric and duodenal ulcers, diverticula of the colon, and to avoid possibility of fecal impaction from barium. Hypaque did not outline mucosal folds as well as barium, but this could be overcome by use of a thickening agent, e.g., gum-acacia.

Booth G

Cholecystokinetic Effect of D-Glucitol in the Normal and the Abnormal Biliary Tract

HARRY TIRSCH, M.D., and SAMSON A. SELEY, M.D., F.A.C.G., Brooklyn, N. Y.

The function of the normal gallbladder is to store bile during the interdigestive periods, to regulate pressure in the biliary passages (in close coordination with the sphincter of Oddi) and to supply the right amount of potent bile to the duodenum. This exhibit reports on a study of 70 patients; 22 patients with normal gallbladders and 48 patients with abnormal biliary tract disease, which include the nonfunctioning gallbladder, postcholecystectomy syndrome, biliary dyskinesia, chronic noncalculus and calculus cholecystitis. D-glucitol, a hexahydric sugar alcohol, given in doses ranging from 4.5 gm. to 18.0 gm. and studied by serial x-ray films, induced a contraction of the normal gallbladder reaching a maximum intensity at the end of 30 minutes. The therapeutic effect of d-glucitol in the abnormal series are demonstrated by means of oral and intravenous cholecystography. In addition to the radiographic findings, the exhibit goes into the dynamics of biliary function and physiology of the hepatobiliary tree.

Booth H

Cardiovascular Dynamics of Bowel Function

ALFRED HALPERN, Ph.D., F.A.C.A., Great Neck, N. Y., PAUL H. KUHN, M.D., F.A.C.A., New York, N. Y., SAUL S. SAMUELS, M.D., F.A.C.A., New York, N. Y. and DAVID SELMAN, M.D., F.A.C.A., Spring Valley, N. Y.

Death after the straining associated with defecation is not a rare phenomenon. Several mechanisms involving the circulation of the heart, pulmonary and peripheral vessels have been suggested in explanation. This exhibit describes the circulatory dynamics observed during defecation of both normal and constipated patients. The data obtained, from several hundred patient measurements, describes the elevation of intrathoracic pressure occurring during straining and its consequent effects on the blood pressure, electrocardiogram circulation time, and the heart rate. It was found that approximately 11 per cent of the efforts of normal subjects were of sufficient magnitude and duration to initiate the classic Valsalva effects of the circulatory system. This incidence was increased approximately fivefold among the constipated subjects. An understanding of some of the precipitating causes for fatal accidents is provided through this systemic study of the circulatory effects associated with defecation, which points toward several methods of avoiding these responses.

Booth J

Sublingual Ergot Therapy in Vascular Headache Associated with Gastrointestinal Symptoms

LESTER S. BLUMENTHAL, M.D., F.A.C.P. and MARVIN FUCHS, M.D., Washington, D. C.

Many clinical entities are accompanied by such profound nausea and vomiting that all medication is promptly rejected or inadequately absorbed. Pyloric spasm of gastric retention can also markedly delay absorption. To circumvent these obstacles, an increasing number of drugs are now being administered by sublingual or rectal suppository methods. Our experience with these routes of drug administration will be presented.

Booth K

Opacifying Gallstones

EMANUEL SALZMAN, M.D., R. P. SPURCK, M.D., L. C. KIER, Ph.D. and D. H. WATKINS, M.D. Denver, Colo.

Certain radiolucent gallstones become radiographically opaque after prolonged administration of some cholecystographic agents with or without x-ray visualization of the gallbladder and the bile ducts (biliary calculography). The condition of prolonged exposure of the calculi to the contrast medium is fulfilled with the "4-Day Telepaque Test"; 3 gm. of Telepaque (Iopanoic Acid) each day for 4 days. A low fat diet is observed during the interval. The opacification of the stones persists for as long as two weeks. The opacification phenomenon has been reproduced *in vitro* and about 20 per cent of all gallstones obtained at surgery or autopsy show this opacifying quality.

Clinically, the vast majority of bile duct stones show this opacifying quality and may be identified by this method. The 4-day Telepaque Test is, probably, the best method available for identifying bile duct calculi in the presence of jaundice. Only a minority of the gallbladder calculi are opacifying. The opacification of biliary calculi after the 4-Day Telepaque Test is the result of a reaction between the contrast medium in the bile and biliverdin on the surface of the stone. The exhibit illustrates the x-ray, pathological and experimental observations involved in the opacification of biliary calculi.

Booth L

A Phase of Postoperative Physiology

TIMOTHY A. LAMPHIER, M.D., F.A.C.G., Boston, Mass.

This exhibit reviews the physiology of the small and large intestines and a new method of reestablishing postoperative bowel function.

With the introduction of new drugs, surgical technics and anesthetics, the problem of postoperative bowel physiology has often been disregarded. The infallible routine in most institutions has been to give a soapsuds enema on the third postoperative day. For too many patients the pain and discomfort of an enema remains in their minds long after other unpleasant symptoms connected with surgery have been forgotten. In addition, the administration of an enema is a time-consuming and disagreeable task for nurses and their aides.

Booth M

Evaluation of a New Cholecystographic Medium

NORMAN ZHEUTLIN, M.D., BERNARD J. O'LOUGHLIN, M.D., Ph.D. and BERTRAM LEVIN, M.D., Los Angeles, Calif.

A new cholecystographic contrast media Orabilex has been evaluated both clinically and radiographically. The results are presented in this exhibit.

Booth N

X-Ray Diagnostic Criteria in Gastric Ulcer

WILLIAM H. BACHRACH, M.D., et al, Los Angeles, Calif.

Based on unselected cases of gastric ulcer in which a team of gastroenterologist, radiologist and surgeon inspected the initial and all follow-up x-rays, a statistical analysis is given of the validity of the following x-ray diagnostic criteria in aiding the differential diagnosis of gastric ulcer: 1. Projects from border. 2. Circumscribed on face. 3. Hampton's line. 4. Associated duodenal ulcer. 5. Relation of width to depth. 6. Preservation of mucosal folds. 7. Radiation of mucosal folds. 8. Smoothness of margins. 9. Air fluid level in crater.

TECHNICAL EXHIBITORS

(Those attending the Convention sessions are urged to take advantage of the time in between the presentation of papers and sessions, to visit the technical exhibits and become acquainted with the many new products and new equipment on display.)

ABBOTT LABORATORIES, North Chicago, Ill. (Booth 20), will welcome members of the medical profession at their exhibit of leading specialties and new products. They have recently introduced a number of new products which their representatives will describe and give information on the results of clinical reports.

AMES COMPANY, INC., Elkhart, Ind. (Booth 27), will feature the latest developments in new, simplified diagnostic products, which are adaptable to routine examination and patient management. The many advantages of the new diagnostic products are quickly demonstrable, and you are cordially invited to stop at their booth to see them.

BURTON, PARSONS & COMPANY, Washington, D. C. (Booth 26), cordially invite you to visit their booth where information, samples and literature will be available for their *EKG Sol*, the modern electrode cream for electrocardiography and electroencephalography, along with their original bulk preparations, *Konsyl* and *L. A. Formula*. *L. A. Formula* contains 50 per cent bulk producing material dispersed in an equal amount of lactose and dextrose. *Konsyl*, on the other hand, contains 100 per cent bulk producing material and is certainly the product of choice for the obese, the diabetic, and others with restricted caloric diets.

CAMERON SURGICAL INSTRUMENT CO., Chicago, Ill. (Booth 2), America's first manufacturer of the Gastroscope, will display their new precision Omniangle Gastroscope. The streamlined design improves the appearance and balance of the instrument. Improved optics provides better viewing, reduces the "blind" area. Reduction of outside lumen (2 mm.) and elimination of all seams and sharp edges, makes Gastroscope easier to introduce. They will also show their complete line of diagnostic instruments.

THE COCA-COLA COMPANY, Atlanta, Ga. (Booth 10). Ice-cold Coca-Cola served through the courtesy and cooperation of the Coca-Cola Bottling Company of Los Angeles and The Coca-Cola Company.

EDER INSTRUMENT COMPANY, INC., Chicago, Ill. (Booth 6), will again exhibit their latest developments in Gastroscopic Equipment featuring especially their new—*Palmer Trans-Esophagoscopic Flexible Gastroscope* with the Bernstein modification as well as other diagnostic equipment of interest to the profession.

ENCYCLOPAEDIA BRITANNICA, Chicago, Ill. (Booth 12).

ENZYME PROCESSING CO., INC., Van Nuys, Calif. (Booth 5).

E. FOUGERA & COMPANY, INC., Hicksville, N. Y. (Booth 11), invites physicians to attend their booth where an exhibit has been prepared on the new oral cholecystographic medium, *Orabilex*. The ever-increasing number of favorable reports published and to be published indicates the growing preference for *Orabilex*. Controlled clinical studies in more than 5,000 cases confirm the diagnostic clarity, absence of patient discomfort and reliability of the single 6-capsule dose.

INSTITUTE OF PUBLIC INFORMATION, New York, N. Y. (Booth 1). Congeners (fusel oil, aldehydes, acids, etc.) are substances found in all alcoholic beverages that provide the taste, bouquet and color. In large amounts, however, congeners may produce toxic effects. This exhibit presents the results of quantitative chemical analyses of congeners found in six leading types of distilled spirits along with correlated acute oral toxicity studies obtained on rats. (Pertinent literature will be available.)

LLOYD BROTHERS, INC., Cincinnati, Ohio (Booth 3). Their professionally trained sales representatives will be happy to greet you and discuss the merits of their products in your practice.

MEAD JOHNSON & COMPANY, Evansville, Ind. (Booth 9), have arranged their exhibit to give you the optimum in quick service and product information. To make your visit productive, specially trained representatives will be on duty to tell you about their products.

NORDSON PHARMACEUTICAL LABORATORIES, INC., Irvington, N.J. (Booth 14), will feature *Ergomar*, a new form of specially processed ergotamine tartrate specifically for sublingual administration in the treatment of recurrent and throbbing type vascular and migraine headache. By-passing the gastric and hepatic enzymatic barriers, *Ergomar* insures more

rapid relief and avoids gastric upset. Also featured *Levonor:* the nonstimulating appetite suppressant. *Levonor's* smooth action permits its use even during the late evening hours without disturbing sleep. Latest reprints are available on *Ferronord Liquid* and tablets, a chelate hematinic providing rapid hemoglobin response without side-effects.

THE PURDUE FREDERICK COMPANY, New York, N. Y. (Booth 24), will present *Senokot:* Constipation corrective containing the concentrated total senna glycosides. *ProBilagol:* Liquid cholecystokinetic for treatment of biliary disease, and *Arthropan:* a new, exceptionally well tolerated antiarthritic, specifically formulated to replace steroid, phenylbutazone, aspirin therapy in arthritis.

REED & CARNRICK, Jersey City, N. J. (Booth 30), will display *Sycotrol,* indicated where fear-anxiety results in somatic complaints referrable to the gastrointestinal tract; and *Modutrol,* which applies the principle of antiphobic therapy as an integrated part of total management for peptic ulcers and other functional gastrointestinal disturbances. Their representatives will be pleased to give you information on these and other Reed & Carnrick specialties.

A. H. ROBINS COMPANY, INC., Richmond, Va. (Booth 23). The peak of the late summer allergy "season" puts *Dimetane* in the featured spot in their exhibit. This unexcelled antihistamine is available in Extentabs, conventional tablets, elixir and in injectable form. Also shown are *Robitussin* and *Robitussin A-C* for cough control, *Robaxin* for relief of skeletal muscle spasm. *Allbee with C,* and *Donnagel.*

WILLIAM H. RORER, INC., Philadelphia, Pa. (Booth 25). *Maalox,* the nonconstipating, pleasant tasting antacid and the new double strength *Tablet Maalox No. 2* are featured. Other product highlights are *Ascriptin,* a rapid-acting professional salicylate, *Chardonna,* an effective antispasmodic, *Parepectolin,* a palatable antidiarrheal preparation, and *Probutylin,* an oral anesthetic for relief from nausea, vomiting, pylorospasm and gastritis. Representatives will be on hand to answer questions about these and their other products.

SANDOZ PHARMACEUTICALS, Division of Sandoz, Inc., Hanover, N. J. (Booth 22), invite you to visit their booth where they will exhibit *Mellaril* the first potent tranquilizer with a selective action (i.e. no action on vomiting centers). This unique action gives specific psychic relaxation with safety at all dosage levels. *Belladenal Space Tabs*—a more effective sustained-action antispasmodic that can be adjusted to the needs of the patient. *BepHan Space Tabs* new approach to prolonged maintenance of low gastric acidity.

G. D. SEARLE & COMPANY, Chicago, Ill. (Booth 18), will feature *Dartal,* the new tranquilizing agent which controls activities associated with anxiety states and other neuroses; *Enovid,* the new synthetic steroid for treatment of various menstrual disorders; *Zanchol,* a new biliary abstergent; *Nilevar,* the new anabolic agent, and *Rolicton,* a new safe, nonmercurial oral diuretic. Also featured, will be *Vallestril,* the new synthetic estrogen with extremely low incidence of side reactions; *Pro-Banthine* and *Pro-Banthine* with *Dartal,* the standards in anticholinergic therapy; and *Dramamine* and *Dramamine-D,* for the prevention and treatment of motion sickness and other nauseas.

SMITH-DORSEY PHARMACEUTICALS, Lincoln, Neb. (Booths 15 & 16). We cordially invite you to witness the demonstration of *Calurin*—a product of Dorsey Research. *Calurin,* a new chemical entity, is highly soluble in gastric juices and avoids the gastric damage so often caused by aspirin. *Calurin*—the freely soluble aspirin—is of major interest whenever analgesia is desired, especially in the treatment of arthritis and rheumatism.

SMITH, KLINE & FRENCH LABORATORIES, Philadelphia, Pa. (Booth 8), will feature: 1—'Stelazine' Tablets, 1 mg. *(New),* for b.i.d. control of anxiety—particularly when expressed as apathy, listlessness and emotional fatigue; 2—*Combid® Spansule®* capsules, for b.i.d., 24-hour relief of both physical and psychic distress in gastrointestinal disorders; and 3—*Prydonnal® Spansule®* capsules, for sustained, uninterrupted antispasmodic-antisecretory-sedative activity.

E. R. SQUIBB & SONS, New York, N. Y. (Booth 31). *Gastrografin,* their Sodium and Methylglucamine Diatrizoates, provides rapid opacification of the alimentary canal in adults, children and infants. Particularly valuable when barium is contraindicated (as in suspected or present obstruction, acute bleeding, tracheoesophageal fistula). Virtually nontoxic on absorption, well tolerated, miscible with blood, does not inspissate. Administer orally, by tube, or rectally.

TRAVENOL LABORATORIES, INC., Morton Grove, Ill. (Booth 17), cordially invites you to view two new products designed specifically for your medical speciality—*Cozyme*, for the physiologic correction and prevention of intestinal atony, abdominal distention, retention of flatus and feces and paralytic ileus, and *Travad*—ready-to-use disposable enema unit featuring a prelubricated tip, 18 inches of flexible tubing and finger tip volume control.

UNITED SURGICAL SUPPLIES CO., INC., Port Chester, N. Y. (Booth 4), will present for the first time to the medical profession, their newly developed series of Three-Dimensional Ostomy Teaching Models. These models fit together mechanically so that anyone can understand the surgical technics involved in each of the ostomy operations. They will prove invaluable in teaching students and nurses the A B C's of ostomy surgery, as well as to explain to a patient about to undergo ostomy surgery, the mechanics of what the surgeon is doing. Also on display will be the complete line of appliances and accessories for Colostomy, Ileostomy, Ureterostomy, and Ileal-Bladder. The new Brunschwig Ileostomy Appliance and Whitmore Ileal-Bladder Bag, both developed by these doctors at Memorial Cancer Center in New York will also be shown. Many of the cancer instruments, devised by Dr. Hayes Martin, Dr. Alexander Brunschwig, and other specialists will be on display. Their representatives will be on hand to answer any of your questions.

WALLACE LABORATORIES, New Brunswick, N. J. (Booth 29). Their representatives will be glad to discuss *Milpath*. *Milpath* (*Miltown* plus anticholinergic) relieves anxiety and tension for enhanced control of pain, spasm, hypermotility and hypersecretion in ulcer and other gastrointestinal disorders. A new potency, *Milpath* 200, has just been made available. It contains only half the *Miltown* but the same amount of tridihexethyl chloride as *Milpath* 400.

WARNER-CHILCOTT LABORATORIES, Morris Plains, N. J. (Booth 7). *Gelusil*—the physician's antacid—for the relief of gastric hyperacidity and management of peptic ulcer. Clinically superior for the peptic ulcer patient because it contains no laxative which might cause irritation and hypermotility. *Pacatal*—clinically proven as a profound ataractic agent, *Pacatal* continues to demonstrate its value in the treatment of mental and emotional disturbances. *Pacatal* is unique in its "normalizing" action, helping the patient to think normally and react in a more stable emotional pattern.

WINTHROP LABORATORIES, New York, N. Y. (Booth 13). New *Creamalin Antacid Tablets* represent one of the most significant improvements in antacid therapy since the introduction of aluminum hydroxide in 1929 insofar as faster, greater and longer acid neutralization is concerned. Tablets are soft, smooth and pleasant to chew and do not cause acid rebound or constipation.

ABSTRACTS FOR GASTROENTEROLOGISTS

STOMACH

HYPOXIA OF ABNORMAL PHYSIOLOGIC ORIGIN AS THE FINAL COMMON PATHWAY IN GASTRODUODENAL ULCER GENESIS: Lt. Col. Eddy D. Palmer and Lt. Col. Jacques L. Sherman, Jr. AMA Arch. Int. Med. 101:1106 (June), 1958.

There are numerous arteriovenous shunts in the gastric mucosa near the muscularis mucosae and in the subserosa of the entire gastrointestinal tract. They might play an important role in the genesis of esophagitis, gastritis and enterocolitis. In this paper only their importance in the genesis of gastrointestinal ulcer is considered. There are direct shunts between small arteries and veins and indirect shunts produced by a specialized channel lined with cells that are able to open and close the shunt by quickly extruding and imbibing fluid (the so-called "Quellzellen" of Schumacher). The shunts divert blood from the mucosal capillaries in case of congestion. The flow in the capillaries is increased by various irritants, drugs, chemicals, as well as by tension, anxiety and resentment. Abnormal shunt function may lead to mucosal hypoxemia and necrosis either by ischemia or by congestion of the capillaries. Local inordinate sensitivity of the shunt mechanism could be responsible for a focal ulcer lesion.

H. B. EISENSTADT

GLOMUS TUMOR OF THE STOMACH: Robert J. Donovan, James H. Graham and Anne R. O'Donnell. J. Internat. Coll. Surgeons 29:699 (June), 1958.

The glomus body consists of two elements, an arteriovenous shunt with afferent arteria and efferent vein and several layers of epitheloid cells surrounding the artery.

This tumor—not infrequently seen in the extremities, especially the nailbeds—is an outspoken rarity in the gastrointestinal tract.

The authors review eight previously published cases, their case represents the ninth one on record.

The patient is a 69-year old female, who had unspecific gastrointestinal complaints. The excellently reproduced x-rays show a radiolucent lesion involving the prepyloric and pyloric part of the stomach. It could have resembled a polyp or a leiomyoma. No free hydrochloric acid was found.

Upon operation a rounded mass was found and a wedge of the stomach includ-

ing the tumor was removed. On microscopical examination this neoplasma was diagnosed as a glomus tumor and because of its benign nature no further resection was done.

This case really represents a medical collectors item.

H. J. JOSEPH

PERFORATED PEPTIC ULCER IN NORTH-EAST SCOTLAND: C. U. Webster and R. D. Weir. Scottish M. J. 3:288 (July), 1958.

The authors made a survey of perforated peptic ulcer in Northeast Scotland from July 1956 to June 1957. One hundred fourteen cases were treated with a mortality rate of 4.4 per cent. One hundred and nine cases were treated with simple suturing; five cases had partial gastrectomy; 51 cases developed postoperative complications.

The majority of perforations were duodenal. All patients were admitted to the hospital within 24 hours.

It was noted that this condition occurred mostly in the summer and usually when the stomach was empty. To obtain more evidence of seasonal incidence the authors reviewed 5 additional years giving a total of 727 perforations and again found that this condition occurred more frequently in the summertime, at the end of the working week.

The family history, mental and physical stress and precipitating factors are gone into in detail.

This series had only 12 female patients, the rest were male patients. The ratio of duodenal to gastric ulcers is high 16–8:1. The diagnosis at times is not easy. A good history is very important in making this diagnosis.

ABRAHAM BERNSTEIN

INTESTINES

HEPATODIAPHRAGMATIC INTERPOSITION OF JEJUNUM, ILEUM, CECUM AND ASCENDING COLON WITH INTESTINAL OBSTRUCTION: David Wyatt Aiken. New England J. Med. 258:1192 (12 June), 1958.

The author discusses the known entity of interposition of intestine between the liver and diaphragm. Emphasis is placed upon the fact that it is almost always a radiologic diagnosis; and much more frequently involves the colon, as opposed to the small intestine; and that it is invariably asymptomatic.

The case reported is apparently the first of its kind wherein the entire jejunum, ileum, cecum and ascending colon were found in the suprahepatic space at the posterior border of the liver. This caused an incomplete high intestinal obstruction which was surgically corrected. Mention is made of the fact that this represents a type of internal hernia which had not been previously categorized as such in the standard classification of internal hernias. In the few other cases where surgery was performed, the extent of involvement was limited to a small segment of small intestine. Also noted in the case report was the presence of aberrant vessels from the fetal umbilical circulatory structures. Brief discussion is made of the possibility of these vestigial remnants being causative agents of the above described disorder.

MORTON SCHWARTZ

PATHOLOGIC FINDINGS AFTER COLON AND RECTAL RESECTIONS: George J. Rukstinat. Am. J. Proct. 9:209 (June), 1958.

The aftermath of surgical treatment of colon and rectal diseases leaves much to be desired. The morbidity and mortality of 39 patients (25 males, 14 females, of similar ages) were studied, comprising a 5-year period. There were 75 operative procedures, including colectomy, anterior resection, abdominoperineal resection, colostomy, and ileostomy. Hospital stay varied from 14 to 33 days.

Extension of bowel tumor was found in 15 cases, of which 8 involved the urinary tract. Half of the male patients exhibited urologic complications. The second com-

monest complication was infection (33 per cent), and next came mechanical defects involving the colostomy. The mortality was 17 per cent, and of the 7 deaths, 2 were due to peritonitis, and 2 to pulmonary embolism.

It is interesting to note that 34 of the 39 patients had bleeding attributed to hemorrhoids, and 12 had hemorrhoidectomies, varying from 22 years to *1 month* prior to operation for bowel tumor. Abdominal pain, however, was the leading symptom, and usually most intense at time of bowel movement.

NORMAN L. FREUND

CUTANEOUS DISEASES OF PERIANAL AND ANORECTAL AREA: Murray M. Robinson. Am. J. Proct. 9:215 (June, 1958.

This paper is a didactic lecture on some perianal cutaneous diseases, many of which are quite rare, such as leprosy, pinta, and yaws, and for most of which there is no treatment given nor available. However, some conditions are worthwhile re-reading at intervals, so that they may be kept in mind.

Fixed drug eruptions are due to habitual intake of phenolphthalein, barbiturates, aspirin, and other coal tar products. The lesions recur in the same site every time the offending agent is ingested.

Acanthosis Nigracans is associated with malignancy in the thorax in 5 per cent, and in the abdomen in the other 95 per cent, therefore most important to recognize. The skin is deeply pigmented and covered with vegetative masses.

Many of the common diseases described are more difficult to diagnose in this area, because the moisture and maceration alter the typical appearances, but a complete examination of the patient will be rewarding.

NORMAN L. FREUND

THE TIGHT ANUS: William Lieberman. Am. J. Proct. 9:229 (June), 1958.

The author classifies anal stenosis into 3 types; spastic, benign or true, and malignant. (The congenital type, quite common, is omitted). The causes of the benign type are given as syphilis, gonorrhea, *lymphogranuloma venereum*, tuberculosis, chronic ulcerative colitis, and trauma. (*Lymphopathia venereum* and chronic colitis may cause rectal strictures, but not anal stenosis, as described by the author). The commonest cause is trauma, usually posthemorrhoidectomy.

Treatment consists of proctotomy, a radial incision through scar or sphincter or both, in the posterior midline. A gauze strip with vaseline is inserted into the wound. Bulky stools and frequent dilatations help maintain the new lumen. On some occasions, an additional proctotomy is also made anteriorly, the reader being cautioned to use good judgment as to when and how deep to go, although no specific mention is made how this may be ascertained. The obvious danger this implies, may be obviated, in the eyes of this reviewer, by resorting to the Martin type of anoplasty, a most simple procedure, which gives excellent results in all cases. The fibrous tissue is incised, the mucosa freed, incised radially, and sutured transversely with 3 sutures. The great majority of eminent proctologists rely on this method exclusively.

NORMAN L. FREUND

AN UNUSUAL MESENTERIC CYST: Laird McNeel. Wisconsin M. J. 57:241 (June), 1958.

A case of mesenteric cyst apparently formed as a result of direct trauma, is presented. Mesenteric cysts are among the rarest of abdominal tumors. There is general agreement that the true mesenteric cyst is a thin-walled structure containing no mucosa and lined by fibroblastic elements containing no muscle fibers and usually filled with chylous or serous fluid, though this case contained gas. The region of occurrence is most commonly the small intestine, especially in the region of the ileocecal valve. The origin of these cysts is obscure.

The diagnosis of mesenteric cysts is usually made on the basis of a movable

abdominal mass, though its position on the mesentery can only be postulated. The symptoms are usually pain, nausea, fullness, and sensation of a mass. Intestinal obstruction and peritonitis have been reported. Treatment is surgical; removal by dissection is the procedure of choice.

ARNOLD L. BERGER

GRANULOMA OF THE RIGHT HALF OF THE COLON (REPORT OF FOUR CASES): Walter A. D'Alonzo. J. Internat. Coll. Surgeons 29: (June), 1958.

Clinically it is difficult to distinguish a benign from a malignant tumor in the gastrointestinal tract.

Granulomatous lesions simulating carcinoma have been described in the literature and the confusing diagnostic problems are emphasized.

The author reviews the literature briefly on this subject and discusses the etiological and pathological picture that it presents. Four cases of granuloma of the right half of the colon are presented in detail together with the pathological picture. These cases were all diagnosed as carcinoma of the colon by x-ray examination and were so treated at the operating table; proved to be granulomata after surgery.

Microscopic examination and special stains did not reveal the cause of these granulomatous lesions.

Annular constricting lesions of the right half of the colon are difficult to differentiate from granuloma and carcinoma.

ABRAHAM BERNSTEIN

PERIODIC FEVER AND ABDOMINAL PAIN: Perk Lee Davis, Margaret H. Shumway and Barbara Siu. Pennsylvania M. J. 61:747 (June), 1958.

A case of a 9½-year old female child with recurrent abdominal pains and temperature elevation since childhood is presented, which, despite repeated and thorough diagnostic maneuvers, remained an occult entity because of the neglect to take an adequate history.

After careful questioning the possibility of epilepsy was suspected and subsequently proven by an E.E.G.

The symptoms thereafter remained well controlled with adequate suppressive therapy.

EZRA J. EPSTEIN

LIVER AND BILIARY TRACT

CORONARY INSUFFICIENCY ASSOCIATED WITH ORAL ADMINISTRATION OF GALLBLADDER DYE: David Littmann and Frank I. Marcus. New England J. Med. 258:1248 (19 June), 1958.

At this V.A. hospital, cholecystography in patients with coronary-artery disease appears to be more hazardous than other comparable diagnostic procedures. These are case reports dealing with males with arteriosclerotic heart disease who experienced fatal attacks of coronary insufficiency soon after the oral ingestion of gallbladder dye. With the possible exception of one case, neither anaphylaxis nor allergy were suggested by the symptoms. Three of the four patients who were very closely observed, showed evidence of increased vagal activity. The symptoms which they presented could either be the cause or effect of the increased vagal tone (bradycardia, sweating, hypotension, nausea, vomiting and diarrhea). According to the authors, atropine or belladonna should be employed in those patients in whom recent symptoms of coronary-artery disease are known or suspected to suppress vagal activity.

IRVIN DEUTSCH

THE PROGNOSIS OF INFECTIVE HEPATITIS: E. R. Cullinan, R. C. King and J. S. Rivers. Brit. M. J. 5083:1315 (7 June), 1958.

In order to evaluate the ultimate prognosis of infective hepatitis a questionnaire was sent to 1,293 males who had served in the Mediterranean campaign of the British

Army where an epidemic of this disease had broken out in 1942. All had suffered an acute attack. For some unknown reason there was a predilection of the disease among officers and among troops in the front line. The mortality rate of the acute attack had been only 0.28 per cent. None of the cases of subacute hepatic necrosis lead to cirrhosis. The files of the Ministry for Pensions were investigated for former war veterans receiving a pension for cirrhosis of the liver; only 4 cases were found where a single acute attack of infectious hepatitis could have been the sole cause of such a chronic liver disorder. The conclusion of these investigators is that cirrhosis develops rarely if at all after an acute attack of infectious hepatitis.

H. B. EISENSTADT

HOSPITAL EPIDEMIC OF HEPATITIS: Frank J. Luparello and Julius Wolf. Am. J. Digest. Dis. 3:436-443 (June), 1958.

Viral hepatitis has been recognized as a common disease among physicians, nurses, and laboratory workers. In several surveys it has been found to be the most common occupational disease among hospital personnel. This paper describes an outbreak over a five and one-half week period affecting four doctors and two nurses on the surgical service of the VA Hospital, Bronx, N. Y. The authors consider it significant that no other case occurred among other personnel, nor in the medical or laboratory services where in the writers' opinion, the degree of exposure to the disease should be greater. As in other surveys the incidence was particularly high among new staff members. The method of transmission was strongly suggested when it was learned that members of the surgical house staff and recovery room nurses shared cups and glasses.

WALTER CANE

THE TREATMENT OF ACUTE CHOLECYSTITIS: C. G. McEachern and R. E. Sullivan. J. Indiana M. A. p. 766 (June), 1958.

From a review of the literature, it is concluded that early surgery is the treatment of choice in acute cholecystitis. Early surgery is distinguished from emergency surgery and it is defined as operative intervention occurring shortly after the diagnosis is established, with fluid and electrolyte balance returned to normal. This method is chosen over conservative management, in which operation is deferred until the acute process subsides or until it is evident that perforation is impending. It is also more advantageous than a program of immediate operation being performed only if the patient is seen early in the attack, but operative intervention being postponed and conservative treatment being carried out for the patient seen later than 48 hours in the acute attack.

Unexpected perforation is considered the strongest argument for early operation in acute cholecystitis. The incidence of perforations in a collected series of 5,272 cases, with 7 individual series reported, varies from approximately 10 to 23 per cent. The mortality in the composite series varies from 17 to 42 per cent. It was also noted that acute cholecystitis occurs twice as frequently in females as in males.

Excluding patients with perforation, the operative mortality rate is 2 per cent in individuals under 70 years of age. This rate compares favorably with the mortality rate of conservative treatment, to which it is necessary to add the mortality rate of later definitive surgery.

JOSEPH E. WALTHER

A REVIEW OF THE CURRENT STATUS OF NONOPERATIVE CHOLECYSTOANGIOGRAPHY: Edwin M. Cohn and David M. Sklaroff. A.M.A. Arch. Int. Med. 101:1051 (June), 1958.

Intravenous cholegrafin visualizes the gallbladder and the bile ducts. Apart from various abnormalities of the gallbladder it may demonstrate common duct dilatation, narrowing, deformity, and displacement. The latter occurs mainly in the presence of pancreatic enlargement. Also residual calculi, gallbladder remnants and a reformed

gallbladder can be seen. Inability to show the common duct may be caused by ductal or by hepatic dysfunction. Biliary dyskinesia is revealed by temporary distention of the common duct at the time of a colic which disappears after nitroglycerin. Cholecystoangiography is of utmost importance in the diagnosis of acute abdominal emergency. The disadvantages of the methods are inconvenience of administration, high expense, reactions to the dye, diagnostic confusion due to unequal opacification of the biliary system or the duodenum. Some opaque or nonopaque stones may escape detection. The terminal portion of the duct is hardly ever clearly demonstrated. Marked jaundice or liver dysfunction interfere with the visualization.

H. B. EISENSTADT

HEPATIC COMA DUE TO EXTENSIVE ISCHEMIC LIVER: Nissim D. Varsano and Johanan H. Boss. Am. Pract. & Digest. Treat. 9:1127 (July), 1958.

These two authors present an unusual study—a heavy hypertensive was admitted to the hospital with stabbing pain between shoulder blades and inability to raise his right leg.

Examination showed B.P. 270/110, irregular pulse of 140 beats per minute, no pulsations in right leg, which was purple-mottled in color, but normal in temperature, other limbs and speech normal.

The history of the pain pattern was that it started between the shoulder blades, radiated to right groin, then over entire abdomen and finally into right leg—thus leading to the suspicion of dissecting aneurysm of aorta below arch.

After ten hours patient became lethargic, with glassy, fixed stare, accompanied by profuse perspiration, mental confusion and total apathy to his worsening condition which seemed to indicate an impending hepatic coma.

Death occurred after 30 hours.

Autopsy showed a tear in the posterior wall of aorta just beyond the ostium of the left subclavian artery, opening into a sac which completely encompassed the aorta down to the right common iliac artery involving the celiac, renal and mesenteric arteries.

The surface and cuts into the liver showed sharply defined yellow areas, the tissue being soft, friable and dry indicating chronic passive congestion throughout the organ.

Microscopic study of the aorta gave the ordinary picture of a dissecting aneurysm.

The sudden hindrance of blood supply to an already passively congested liver probably accounts for the hepatic coma death of this patient, when the aneurysm involved the celiac artery and its three main branches.

J. EDWARD BROWN

ACUTE EMPHYSEMATOUS CHOLECYSTITIS: A CASE REPORT AND REVIEW OF THE WORLD LITERATURE: Alfred Edinbaugh and Abraham Geffen. Am. J. Surg. 96:66 (July), 1958.

Acute emphysematous cholecystitis is a rare pathological condition of the gallbladder characterized by the growth of gas-producing organisms within a gallbladder, the seat of an acute cholecystitis. The presenting clinical picture is usually indistinguishable from that of an acute cholecystitis. The diagnosis is actually made by roentgen studies of the abdomen which demonstrate a distended gallbladder with air in its lumen and or within its wall.

This is the 50th case reported in the medical literature of the clinical and pathological entity known variously as acute pneumocholecystitis, pyopneumocholecystitis, acute gaseous cholecystitis, gas gangrene of the gallbladder and emphysematous cholecystitis.

The diagnosis was made by x-ray findings in 43 cases in which preoperative films were taken, and in the other seven cases, the diagnosis was made at operation. An abdominal film shows gas in the lumen of the gallbladder, in its walls, or in the pericholecystic tissues. Frequently, no gas is seen until 24 to 48 hours after the onset of the acute attack; serial films are therefore of great significance.

At operation there is usually a tense, distended gallbladder with acute and chronic changes in the walls. There is gas under pressure in the lumen, and a foul

smelling or purulent exudate. Biliary calculi are present in a great majority of gallbladders. Pericholecystic abscess is a very frequent occurrence—in 27 of the 38 cases operated upon (71 per cent), and might be considered part of the pathological process, if it is allowed to fully develop.

CARL J. DEPRIZIO

SURGICAL MANAGEMENT OF PRIMARY AND METASTATIC CANCERS OF THE LIVER: George T. Pack. Northwest Med. 57:881 (July), 1958.

In 1930 an analysis of 20,000 case histories of cancer indicated that only 0.17 per cent of admissions were for primary cancer of the liver.

The surgeon who plans to do major extirpative surgery for tumors of the liver should be thoroughly familiar with the vasculature of the organ. The author outlines sound principles for removal of tumors of liver even to resection of the lobes where tumors are located.

Cancer of the gallbladder has been a problem because we have not been familiar with the phenomenon of metastasis within the liver. A cancer that is only superficially invading the surface of the liver may very shortly have secondary and tertiary deposits within the liver parenchyma. Because of this frequent occurrence and the very low cure rate for gallbladder cancer by cholecystectomy and excision of the gallbladder bed, we have advocated and practiced total right hepatic lobectomy for all gallbladder cancers or, as in two recent cases, middle lobe hepatectomy has been performed and it is hoped this may prove to be a useful procedure for gallbladder cancer. The gallbladder is removed in continuity with the middle lobe.

As a palliative measure surgery is indicated and it is sometimes worthwhile to attack metastatic cancer within the liver.

Patients who have had a major hepatectomy tend to have marked hypoproteinemia and one needs to be very careful about giving them the proper diet rich in protein —by mouth, absorbed through the intestinal tract and carried into the portal system up to the liver where it can be used.

The liver has an irresistible urge to regenerate itself. A human with less than 20 per cent of liver substance may regenerate substance as large even as a normal liver.

I. HENRY EINSEL

PANCREAS

ATYPICAL SYMPTOM-SIGN COMPLEX OF ACUTE PANCREATITIS: J. L. Donhauser and Nolton H. Bigelow. Am. J. Surg. 96:61 (July), 1958.

When one considers the supposed cardinal symptoms and signs of massive, acute pancreatitis, abdominal pain, vomiting and shock of varying degrees are looked upon as typical of this disease. Some severe instances causing death within a few hours or a few days, show little of the picture of the "pancreatic drama".

An analysis of the clinical records of 21 cases verified by autopsy, was therefore undertaken to ascertain how often an accurate diagnosis was made, or at least how often it reasonably could have been made. Instances of massive, acute pancreatitis of sufficient severity to be considered the major cause of death, were relatively rare, only 21 cases being present in some 10,000 autopsies.

That so little consideration was given to the possibility of the existence of acute pancreatitis, is demonstrated by the fact that in only six cases was the amylase determination made. This test should be done very early in the course of the disease. The pain pattern is so variable that in any kind of upper abdominal disorder of uncertain or obscure nature, an amylase determination should be made. Varied diagnoses were made, such as, coronary occlusion, cardiac insufficiency, intestinal obstruction, arteriosclerotic disease, chronic alcoholism, biliary tract disease, splenic infarct and perforated gastric ulcer.

Abdominal tenderness is very commonly found. Tenderness was noted in 15 patients. There was no tenderness in one patient, and of five others, no mention is made. Electrocardiogram was noted as abnormal in 10 cases and questionable in one. Eight patients were clinically diagnosed as affections of the heart. Shock was present in only 3 of the 21 cases. The average

systolic pressure for the entire series was 128 mm.

A review of the 21 cases, with findings at autopsy and clinical notes, compel the writers to seriously consider the direct relationship between this disease and the vascular system.

CARL J. DEPRIZIO

ACUTE PANCREATITIS WITH PERITONEAL FAT NECROSIS—ROENTGEN DIAGNOSIS: T. B. Merner. Am. J. Roentgenol. 80:67 (July), 1958.

This article stresses the importance of new additional signs of peritoneal fat necrosis. The important x-ray finding is that of mottled areas of increased density from one to three cm. in diameter, scattered throughout the abdomen, and representing fat necrosis with saponification.

Severe pancreatitis, with obstruction of the pancreatic duct, frequently is present with resulting extrusion of excess pancreatic enzymes into the pancreatic tissue. This produces marked destruction of the necrosis of the pancreas with release of the enzymes into the peritoneal cavity. Rapid transformation of fatty tissues into the calcium soaps by combination with calcium from the blood serum results. The greater density, islands of calcium soaps in necrotic areas, in contrast with more normal areas, produces a mottled appearing shadow in the roentgenogram.

VINCENT J. GALANTE

GAS IN THE PANCREAS AS A SIGN OF ABSCESS: J. W. Angos and R. B. Holmes. Am. J. Roentgenol. 80:60 (July), 1958.

Abscesses of the pancreas may occur in association with an acute chronic pancreatitis and generally a complication of a penetrating peptic ulcer. Symptoms and constant elevation serum amylase will usually indicate development of a pancreatic cyst. The abscess may be localized in the pancreas itself or in one of the spaces of the abdomen such as lesser sac or mesocolon. Roentgen findings are those of gas extending to the right of the mid line, separated from the right hemidiaphragm by the liver. Less frequent changes of the pancreatitis with abscess formation is characterized by a small collection of gas. Abscesses associated with pancreatitis may remain with the substance of the pancreas, and therefore are small and moderate in size, others extend beyond the confines of the pancreas to nearby sites, have been known to perforate into the stomach, duodenum and colon. Lesser common roentgen signs of abscess with pancreatitis are the obliteration of the psoas outline, calcification, sentinel loop of distended small bowel, distorted duodenum mucosal pattern, extrinsic pressure defects on the stomach and duodenum.

The most common direction of the spread of the pancreas abscess is into the lesser peritoneal sac, which lies anterior to the pancreas. In this large space the inflammation may spread widely and produce a large mass. In such instances a long air fluid level indicating the diameter of the abscess cavity may be seen, on routine roentgen studies. When the gas is confined to the pancreas, it is unlikely to be seen as a unilocular cavity, with a single air fluid level, gas is more likely to be dispersed among the solid material and to produce a mottled appearance. This is not diagnostic and may be seen in any abscess of other viscera or other connected tissues.

VINCENT J. GALANTE

PATHOLOGY AND LABORATORY RESEARCH

EFFECT OF DIOCTYL SODIUM SULFOSUCCINATE ON BOWEL FUNCTION IN MENTAL PATIENTS: Darwin K. Phelps. J. Indiana State M. A. 51:646 (May), 1958.

The study concerned a group of 130 hospitalized mental patients who had a long-standing history of chronic functional constipation necessitating administration of medication or enemas for bowel evacuation.

Fifteen c.c. of dioctyl sodium sulfosuccinate 1 per cent solution, given in orange

juice once daily, was effective in obtaining a soft stool in all patients. Within six weeks of treatment the dosage was successfully reduced to 5 c.c. and in the great majority of patients, no medication was necessary beyond 8 weeks treatment.

Administration of the material, which acts by lowering interfacial tension, resulted in great reduction in number of enemas required by bedridden patients and improved the efficacy of enemas when these were still necessary.

JOSEPH E. WALTHER

EXPERIMENTAL STUDY ON TRAUMATIC LESION OF THE PANCREAS AND TREATMENT OF ITS CUT-END: I. EXPERIMENTAL STUDY ON TRAUMATIC LESION OF THE PANCREAS: Shigeki Nishida. Arch. f. Japan. Chir. p. 707 (May), 1958.

In a series of animal experiments, the pancreas was subjected to various mechanical injuries and end results investigated. The authors come to the following conclusions. 1. Pancreatic injuries caused by trauma or surgical procedures may result in localized or diffuse peritonitis depending on the localization and extent of injury to the pancreatic ducts. 2. Peritonitis is caused by the irritation and fatty necrosis resulting from the release of trypsinogen from the injured duct. Although inactive while in the duct, trypsinogen converts to active trypsin on coming in contact with various organic and inorganic substances when the duct is severed. 3. Secretin, morphine, pilocarpine and physostigmine promote, while barbituates and atropine inhibit pancreatic secretions. 4. Where food or medicaments that promote pancreatic secretion are given the intraabdominal changes are more severe. Where the injury to the pancreas is very severe contrary to expectations, the intraabdominal changes are mild irrespective of medicaments or food given.

A. J. BRENNER

TUBELESS GASTRIC ANALYSIS: M. A. Denborough, F. P. Retief and L. J. Witts. Brit. M. J. 5081:1213 (24 May), 1958.

The authors describe in detail the methods used in determining gastric acidity by the tubeless method. They compared the results of Diagnex using caffeine sodium benzoate as the gastric stimulant and using either quinium or the orthoquinoid salt of azure blue, with the standard test using a tube and histamine as a stimulant. The quinium test showed satisfactory agreement with the standard single test meal of histamine. False positives and false negatives were more frequent with the azure blue test when the results were compared with the augmented histamine test meal. They concluded that the quinium test is a valuable method for screening patients for achlorhydria. They include a review of the literature.

ABE ALPER

PARENTERAL ADMINISTRATION OF FATS: II. CLINICAL APPLICATION OF FAT EMULSION: Yorinori Hikasa et al. Arch. f. Japan. Chir. p. 736 (May), 1958.

Until recently nutritional value of fat has not been adequately recognized since it was thought that carbohydrate and protein could be substituted for fat. It has now been adequately demonstrated that fat has nutritional values and advantages which can not be substituted for by protein or carbohydrates. Daily requirements of fat has become an important problem in nutrition of the well, and more so of the sick.

The authors have recently introduced "Fatgen" which is a 20 per cent solution of sesame oil in emulsion. When given intravenously in combination with Ringer's solution there are no side-effects. Multivitamins may be added to the infusion. This preparation has been found to cause a remarkable protein-sparing effect. Administration of this emulsion has also caused an actual increase in body weight. Fat emulsion infusions help maintain the normal level of plasma colloidal osmotic pres-

sure. In healthy adults no changes were noted in the circulating plasma volume and extracellular fluid volume following repeated intravenous infusions of Fatgen.

A. J. BRENNER

EPIDEMIC INFANTILE GASTROENTERITIS: J. Brodie. Scottish M. J. 3:214 (May), 1958.

It is well known that infantile gastroenteritis is caused by specific strains of *E. coli*. Because of the high incidence of these strains in the stools of infants receiving a specific type of saccharose supplemented dried milk, the authors attempted to determine whether or not this milk contained any substance which facilitated the growth of these organisms. They used different sugar media in growing the various strains of *E. coli*.

The results showed that in the media with milk alone or milk with added lactose, glucose, or maltose, the nonpathogenic coli outgrew the pathogenic strains. In the instances in which saccharose was added however, the organism which fermented saccharose more rapidly appeared to grow the fastest. In most of these cases, the organism was a pathogenic one.

THEODORE COHEN

THE CLINICAL SIGNIFICANCE OF SERUM CYANOCOBALAMIN (VITAMIN B_{12}) IN LIVER DISEASE: M. Rachmilewitz, Y. Stein, J. Aronovitch and N. Grossowicz. A.M.A. Arch. Int. Med. 101:1118 (June), 1958.

Serum concentration of Vitamin B_{12} has been found to be elevated in acute and chronic liver disease associated with hepatic damage. The greatest rise occurs during the initial phase of acute viral hepatitis. The Vitamin B_{12} level falls during the 3rd or 4th week, but elevation persists as long as the disease remains active. The highest values are found in acute yellow atrophy of the liver. In chronic liver diseases, especially cirrhosis, the elevation of serum cobalamin depends on the activity of the parenchymal disease. Normal values are found in obstructive jaundice unless secondary hepatocellular involvement has occurred. Therefore, this test is of value in differentiating hepatic and extrahepatic jaundice. Normal levels of Vitamin B_{12} were also found in primary biliary cirrhosis and in chlorpromazine jaundice as long as there was no hepatic cell necrosis.

H. B. EISENSTADT

FECAL OCCULT BLOOD TESTS WITHOUT DIETARY RESTRICTIONS: R. L. Smith. Brit. M. J. 5083:1336 (7 June), 1958.

Any test for the detection of occult blood in the stool without preparation of the patient with a meat-free diet must have a low sensitivity, otherwise too many false-positive results would be obtained. In the attempt to find the best compromise between incidence of false-positive results and sensitivity, various dilutions of orthotolidine were tested and a 5 per cent solution was found to be most suitable for this purpose. It gave only 10 per cent false weakly positive results. All strongly positive reactions with this method were highly significant. In addition, both occultest and hematest tablets were investigated. Both tablets were useful for the same purpose. Occultest tablets were preferred because hematest tablets sometimes turned pale blue with the addition of water alone in the absence of contact with a stool specimen.

H. B. EISENSTADT

THE SIGNIFICANCE OF HYPERAMYLASAEMIA IN SURGICAL CONDITIONS: D. W. Short. Scottish M. J. 3:305 (July), 1958.

In order to determine the value of serum amylase as a diagnostic aid in acute abdominal conditions, the authors present results from 181 cases of acute abdominal symptoms and 100 cases without acute disease. The method of performing the test is gone into in great detail. The survey showed that a high serum amylase of over

1,000 mg. per cent within the first few hours of an acute abdominal condition, not complicated by renal failure or morphine sedation, is indicative of acute pancreatitis. Eight cases of acute pancreatitis were partly diagnosed on the result of the serum amylase test.

The serum amylase levels were studied in perforated ulcer, acute appendicitis, and in biliary tract disease.

The mechanism of hyperamylasemia and its significance is discussed. The literature is carefully reviewed.

The serum amylase test is a biochemical procedure, its results are particularly significant in making a diagnosis of acute pancreatitis.

One should keep this test in mind in every acute abdominal condition.

ABRAHAM BERNSTEIN

SERUM ENZYMES IN DISEASE: I. LACTIC DEHYDROGENASE AND GLUTAMIC OXALACETIC TRANSAMINASE IN CARCINOMA, II. LACTIC DEHYDROGENASE AND GLUTAMIC OXALACETIC TRANSAMINASE IN ANEMIA: Michael West and Hyman J. Zimmerman; Hyman J. Zimmerman, Michael West and Paul Heller. A.M.A. Arch. Int. Med. 102:103 & 115 (July), 1958.

Lactic dehydrogenase was frequently elevated in cancer patients, especially in the presence of metastatic dissemination. This increase of enzyme occurred in the absence of liver involvement while the increase of SGOT indicated liver invasion. Only rarely SGOT was elevated by metastases to the heart muscle. SGOT elevation may be the only abnormal liver function test in metastatic cancers.

Lactic dehydrogenase was markedly increased in megaloblastic anemia, sickle cell anemia, leukemia lymphoma and infectious mononucleosis without hepatic involvement. However, SGOT elevation always indicated that the liver was affected by disease.

H. B. EISENSTADT

THE USE OF SERUM PROTEIN ELECTROPHORESIS IN CLINICAL MEDICINE: Robert L. Wall. A.M.A. Arch. Int. Med. 102:618 (Oct.), 1958.

Paper electrophoresis may be a useful adjunct in the differential diagnosis of jaundice and of various hepatic diseases without jaundice. Cholecystitis for instance leaves the protein pattern unchanged, while common duct obstruction has an increased beta-lipoprotein. Viral hepatitis shows changed curves in the initial stage. At first there is an increase of alpha 2, later a decrease of albumin, and finally a marked increase of gamma globulin. Chronic liver disease, lupoid hepatitis, cirrhosis and other advanced parenchymal disorders show a marked decrease of albumin, a decrease or increase of alpha-1 globulin, normal or decreased alpha-2 and beta globulins and a marked increase of gamma globulin. Biliary cirrhosis is characterized by a marked elevation of beta lipoproteins. Primary and metastatic cancer causes a decrease of albumin, an increase of gamma globulin and a decrease of beta lipoproteins. Lymphomas, leukemias and other diseases of the reticuloendothelial system which may affect the liver have marked hypogammaglobulinemia. Multiple myeloma and various macroglobulinemic conditions show an abnormal peak between beta and gamma the so-called M peak of paraprotein.

H. B. EISENSTADT

BOOK REVIEWS FOR GASTROENTEROLOGISTS

1957-58 YEAR BOOK OF PATHOLOGY AND CLINICAL PATHOLOGY: Edited by William B. Wartman, B.S., M.D., Morrison Professor of Pathology, Northwestern University; Director of Laboratories, Passavant Memorial Hospital; Senior Attending Pathologist, Chicago Wesley Memorial Hospital, etc., etc. 478 pages, 171 figures. The Year Book Publishers, Inc., Chicago, Ill., 1958. Price $8.00.

As in previous years, the book is divided into two sections, Pathology and Clinical Pathology. The text covers the entire human system plus various other items of interest to all practicing physicians, pathologists and laboratory workers.

It is highly recommended as are all other Year Books.

PEPTIC ULCER AND PSYCHOANALYSIS: Angel Garma, M.D., Buenos Aires, Arg. 148 pages. Williams & Wilkins Company, Baltimore, Md., 1958. Price $6.00.

In 13 chapters, the author discusses the neurologic and psychologic aspects of ulcers of the stomach and ulcer-like symptoms unrelated to a definite ulcer lesion. For the clinician who wishes to enhance his knowledge and to apply the various aspects of psychoanalysis, the book will be a mine of information. Others who are disinclined to dabble in psychoanalysis will find that in addition to medical and dietotherapy, referring some of the patients to a neuropsychiatrist will aid in curing the patient.

The chapter on ulcers and pseudoulcers, the summary and the bibliography, complete the book.

All physicians will find it a worthwhile reference.

THE PASTEUR FERMENTATION CENTENNIAL—1857-1957: A Scientific Symposium on the occasion of the 100th anniversary of the publication of Louis Pasteur's Memoire sur le fermentation appelee lactique. 207 pages. Chas. Pfizer & Co., Inc., New York, N. Y., 1958.

Thanks to the Pfizer organization for this interesting book about Pasteur. His theories and scientific studies have aided present day medicine by leading to one of the most useful therapeutic agents, the antibiotics. Physicians who are interested in the history and the progress in medicine are advised to read this book.

A CLASSIFIED BIBLIOGRAPHY OF GERONTOLOGY AND GERIATRICS—SUPPLEMENT ONE—1949-1955: Nathan W. Shock, Chief, Gerontology Branch, National Heart Institute, National Institutes of Health and the Baltimore City Hospitals. 525 pages. Stanford University Press, Stanford, Calif., 1957. Price $15.00.

An extensive volume with selection and classification of the references dealing with Gerontology. It represents the cooperative efforts on the important problems of ageing.

Physicians and research workers who are interested in Gerontology, will find here a handy reference to journals, subject index, and authors index culled from various medical publications and especially from the Journal of Gerontology.

DISEASES OF THE LIVER AND BILIARY SYSTEM—SECOND EDITION: Sheila Sherlock, M.D. (Edin.); F.R.C.P. (London), M.R.C.P. (Edin), Physician and Lecturer, Department of Medicine, Postgraduate Medical School, University of London. 719 pages, illustrated. Charles C. Thomas, Springfield, Ill., 1958. Price $11.50.

Among the more recent books published on liver and biliary diseases, Dr. Sherlock's volume covers the subject thoroughly. Thirty-one chapters, extensive references, a cross index, numerous illustrations, tables and line drawings, laboratory and other details, should appeal to all physicians.

The reviewer recommends it highly.

THE ESOPHAGUS, MEDICAL AND SURGICAL MANAGEMENT: Edward B. Benedict, M.D., F.A.C.S., Assistant Clinical Professor of Surgery, Harvard Medical School; Endoscopist, Massachusetts General Hospital and George L. Mardi, M.D., F.A.C.S., Clinical Associate in Surgery, Harvard Medical School, Assistant Surgeon, Massachusetts General Hospital. Foreword by Edward D. Churchill, M.D., F.A.C.S. 390 pages, 16 color plates and 108 black and white illustrations. Little, Brown & Company, Boston, Mass., 1958. Price $15.00.

A concise and comprehensive text dealing with the normal and abnormal conditions of the esophagus written by Drs. Benedict and Mardi, is highly recommended for all physicians and especially gastroenterologists and roentgenologists.

Esophagoscopy, its indications, contraindications, medical and surgical treatment and drug therapy enhance the value of the monograph.

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Supplied: 3 mg. tablets in bottles of 100.

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Clinical Diagnosis	Oxyphencyclimine*	ENARAX†
Peptic ulcer	448	48
Gastritis	16	17
Gastroenteritis	—	35
Colitis	37	—
Duodenitis	6	3
Functional bowel syndrome	14	—
Hiatus hernia (symptomatic)	16	1
Pylorospasm or cardiospasm	11	2
Irritable bowel	11	—
Biliary tract dysfunctions	11	1
Miscellaneous	7	29
Total number of patients	569	156
Clinical Results *Excellent*	445	150
Fair	56	—

* **Oxyphencyclimine alone**—clinically effective in 87% after a year's testing.

† **ENARAX** (oxyphencyclimine plus ATARAX)—all successful cases in "excellent" category.

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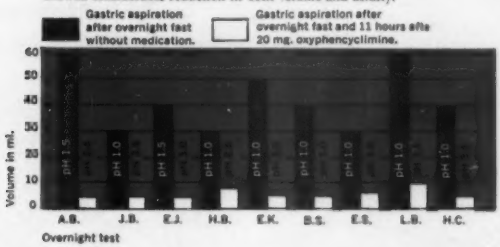
Tests conducted in 9 representative ulcer patients after overnight fasts showed considerable reduction in both volume and acidity.



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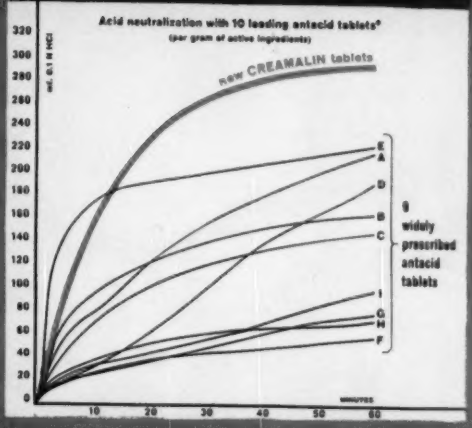

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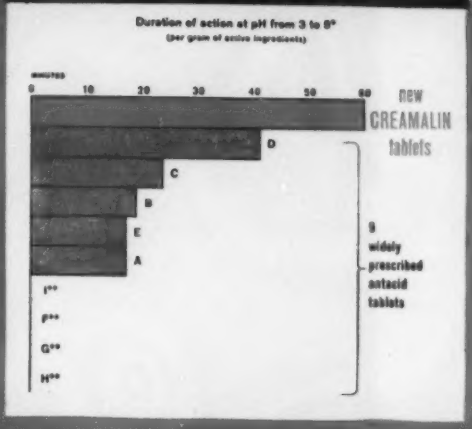

*Friedel, E. T., Jr., Fisher, and Talmer, M. L. A new highly reactive aluminum hydroxide complex for gastric hyperacidity. To be published.
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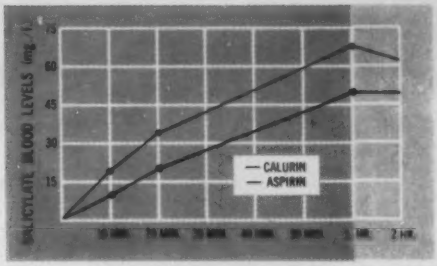

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CALURIN is the aspirin of choice, especially when high-dosage, long-term therapy is indicated:

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Dosage: Each tablet of Calurin is equivalent to 300 mg. (5 gr.) of acetylsalicylic acid. For relief of pain and fever in adult patients, the usual dose of Calurin is 1 to 3 tablets every 4 hours, as needed; in arthritic states, 2 or 3 tablets 3 or 4 times daily; in rheumatic fever, 3 to 5 tablets 4 or 5 times daily. For children over 6 years, the usual dose is 1 tablet every 4 hours; for children 3 to 6 years, ½ tablet every 4 hours, as required. Not recommended for children under 3.

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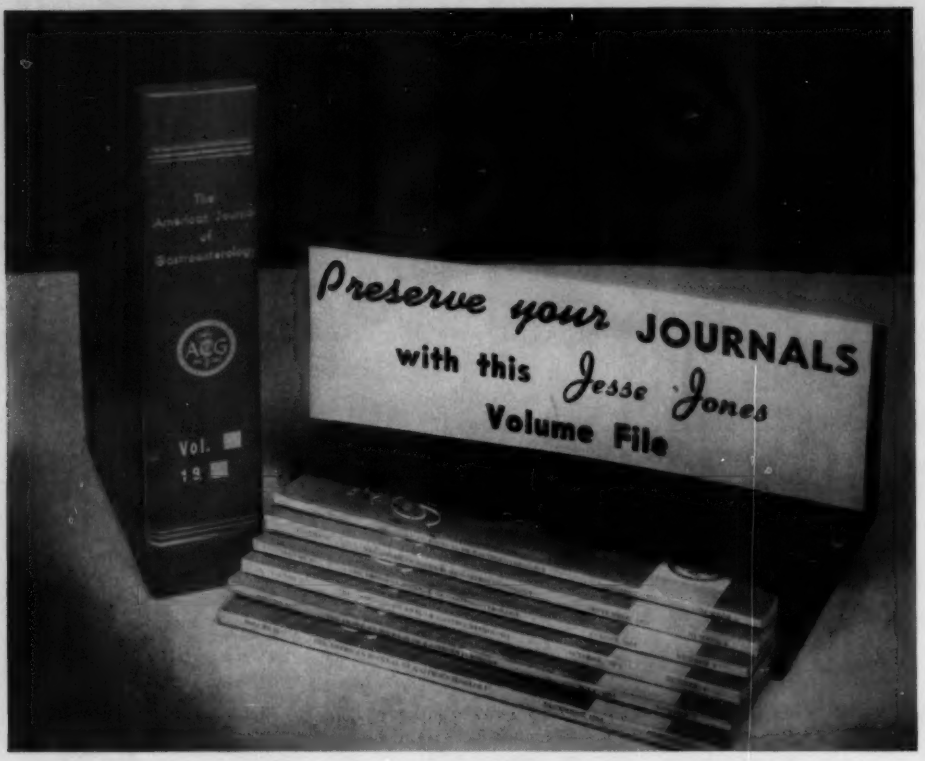

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1. Case reports on file, Wyeth Laboratories. 2. Parks, R.V., and Moessner, G.F.: Dual Approach to Patient Care, Scientific Exhibit, A.A.G.P., April, 1959.

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1. Chamberlin, D. T.: Gastroenterology 17:224. 2. Hufford, A. R.: Am. J. Digest. Dis. 19:257. 3. Cholst, M., Goodstein, S., Berens, C. and Cinotti, A.: J.A.M.A. 166:1276, 1958.

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